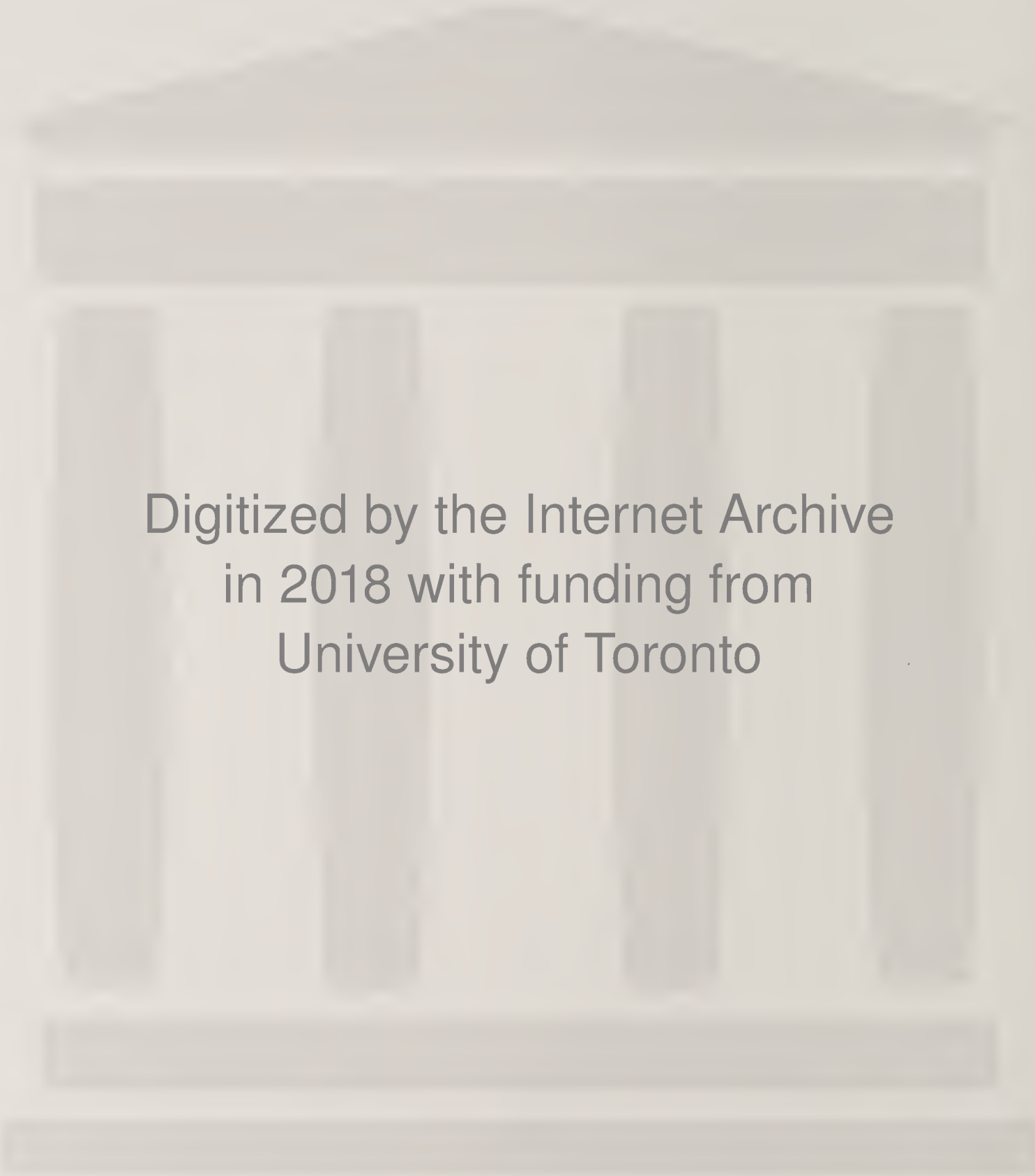




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With great excitement, we present the first issue of the *University of Toronto Medical Journal (UTMJ)* in its seventy-fifth year of publication. To celebrate this occasion, the *UTMJ* has been redesigned and several new sections have been added to give North America's oldest student-run medical journal new dimensions that reflects both its heritage and progressive view of medicine.

In preparing this edition of the *Journal*, it has been our goal to develop a mandate for its future. Since 1923, the primary focus of the *UTMJ* has been the publication of high quality, peer-reviewed, student research and review articles. We believe that this year the *UTMJ* examines and modernizes the initial goals put forth at its inception and supplements them with a set of new long-term objectives. Our intention is to provide future *UTMJ* staff with an editorial framework upon which improvements can be made while maintaining the *Journal's* conceptual continuity.

In keeping with *UTMJ's* mandate for quality, our review process now includes members of the University of Toronto Faculty of Medicine in the Editorial Board. Also in continuity with the *Journal's* tradition, articles pertaining to a wide variety of disciplines and interests including pediatrics, cardiovascular pathology, clinical epidemiology, medical imaging, and preventative medicine have been included. This issue's feature article reviews failure to thrive, a symptom and sign (but *not* a disease) of impaired development of the very young. News & Views, Book Reviews, and Technology Reviews are sections that will be featured in each issue of this year's *Journal* to keep readers up to date on trends and perspectives in science and medicine; Clinicopathological Correlation and Quick Diagnosis are sections which we include to exercise the diagnostic muscles of even the most astute clinician.

Two new sections are featured in this edition of the *UTMJ*. To celebrate our seventy-fifth year of publication we have added From the Archives, comprised of historically interesting and memorable articles published in past issues of the *UTMJ*. In this issue, the lighthearted articles on personality in medicine, and the creation of Pabulum offer contrast to the notice from 1934 of the opening of the new Women's College Hospital, Canada's first institution dedicated to women's health which today faces imminent demise. Another addition to this year's *Journal*, and a potential favourite for all budding internists is Morning Report. Blending the classic Oslerian method of correlating physical findings with diagnosis and modern diagnostic techniques such as real-time medical imaging, this section features a clinical dialogue that offers readers a window on how an expert physician thinks through a case.

This year the *UTMJ* aims to broaden its readership and authorship. Accordingly, we are soliciting submissions from students across Canada and the United States and we are maintaining and improving our fledgling WebSite (<http://icarus.med.utoronto.ca/mjweb/www.mjweb.htm>). Without further delay, we welcome you to our first of three issues and encourage you to send us your comments to Letters to the Editors, (mike.angel@utoronto.ca or christine.brezden@utoronto.ca). We hope you enjoy Volume 75, No. 1.

Michael J. Angel, Ph.D
Christine B. Brezden, Ph.D
Editors-In-Chief

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Failure to Thrive: Approach to Diagnosis and Management

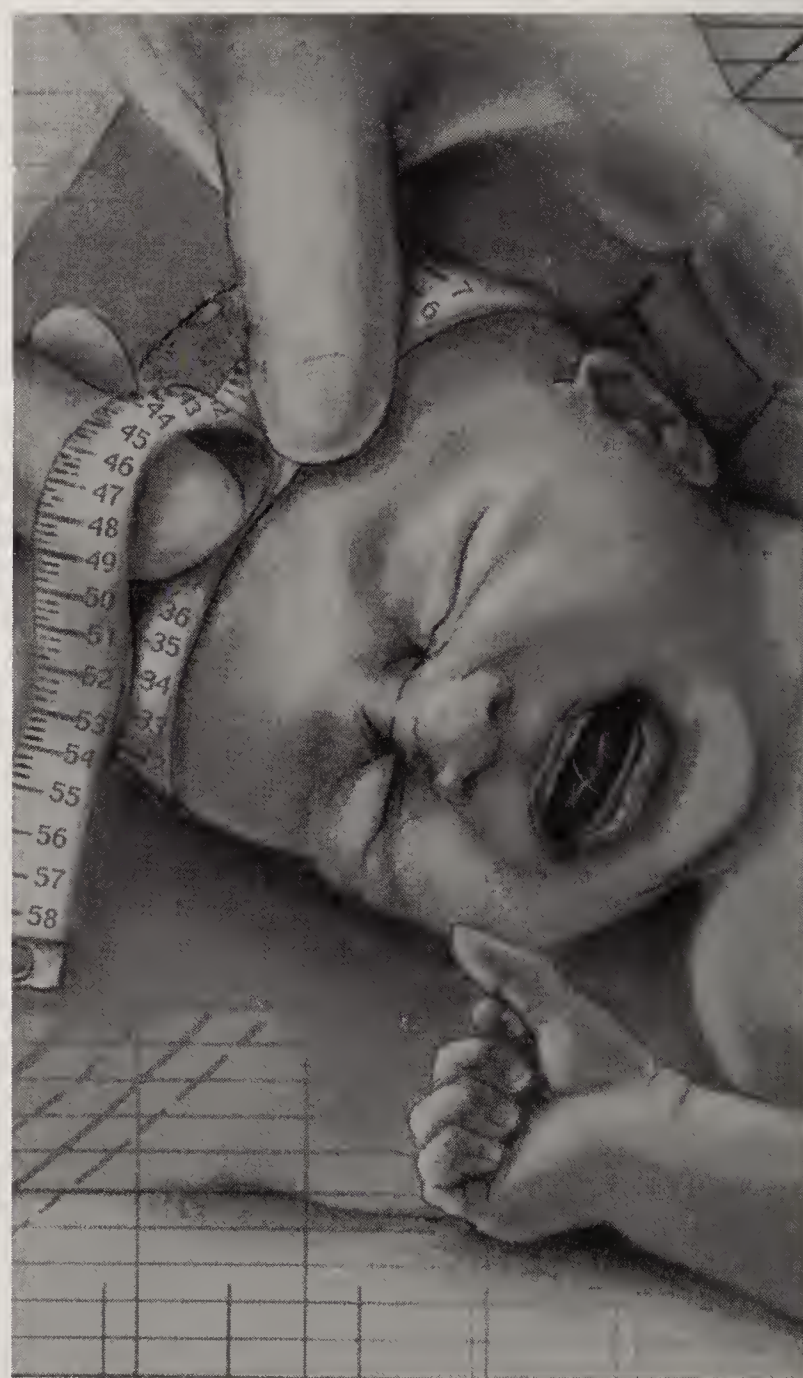
Adam Cheng (9T9) and
Sheila Jacobson, MBBCh, FRCPC*

Abstract

Failure to thrive (FTT) in infants and young children can be a perplexing presenting complaint to those without a structured and organized approach to the problem. Primary care physicians and pediatricians play an integral role in the accurate diagnosis and management of this problem. A thorough assessment of the child begins with a proper history and physical examination, and ideally, also includes the observation of a feeding session with the parents and child. This information helps the physician classify the cause of the growth deficiency, and subsequently decide whether or not lab investigations are necessary. Management of FTT may include dietary support, multidisciplinary support or hospitalization in severe cases. This review article presents the definition and classification of failure to thrive, a simple and organized approach to diagnosis and management, and the expected prognosis and outcome of children suffering from FTT.

Introduction

Failure to thrive (FTT) or growth deficiency, a problem commonly encountered in the general pediatrician's office, can be both puzzling and frustrating to solve without an efficient approach to diagnosis and management. The extensive differential diagnosis of FTT at times can make it seem like a daunting complaint, especially in the presence of parents who are worried about their young child. FTT seems to be more frequently found in lower socioeconomic classes but can affect



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children from all backgrounds. It accounts for up to 1% of all pediatric hospitalizations in the general population.¹ In the United States, this figure is higher in families with medical and psychosocial problems or with low socioeconomic status, as up to 10% of children in these families were found to have FTT.²

Definition

In order to discover the cause of a child's growth deficiency, one needs an organized and thorough approach to the situation. This begins with the proper identification of FTT. It is important to recognize that FTT is a sign or symptom, and not a disease. It can be defined as one of the following: (a) a child whose weight is consistently below the third percentile for that age;³ (b) a child whose weight is less than 80% of the ideal weight for that age;⁴ or (c) a child whose decreased growth has crossed two major growth percentiles in a short period of time.⁵ Generally speaking, the term is used to describe infants and young children whose growth is considerably less than that of their peers.

Weight, height and head circumference classically are assessed by using standard charts, which unfortunately have several drawbacks. Normally, these charts are standardized for populations predominantly of European ancestry. They do not account for genetic endowment, and are not appropriate for premature babies or babies with genetic syndromes (c.g. Down Syndrome). For the first two exceptions, the physician must be aware of slight variants of the normal standard accounted for by genetics or racial background and not misdiagnose these children as having FTT. Premature babies and syndromic babies should be plotted on appropriate charts.

Children who are malnourished gradually fall off normal curves for weight first, then height, and if severely malnourished, then head circumference. From this statement we can infer that a low weight for age alone suggests acute malnutrition, while a low weight and height for age suggests chronic malnutrition.¹

Classification and Etiology

Failure to thrive can be classified into one of three etiological categories: organic, non-organic, or mixed etiology. Separate from these three categories is "factitious FTT,"⁶ which includes other diagnostic considerations often confused for growth deficiency, namely familial short stature and constitutional growth delay. Factitious FTT should be considered a normal physiological variant and should not be diagnosed as FTT.

Organic FTT is defined as growth deficiency caused by a specific medical illness. Although organic causes are responsible for less than 5% of FTT in the outpatient setting,⁷ this percentage rises dramatically to 70% when weight, height and head circumference are all below the third percentile.⁴ Non-organic causes account for the majority of FTT cases encountered in the community. Specifically speaking, non-organic FTT refers to growth deficiency without a diagnosable medical etiology. Often there is no evidence of systemic disease, no abnormal laboratory findings, and pronounced environmental and psychosocial disruption within the family.⁸ Non-organic failure to thrive may be associated with delayed development

and abnormal behaviour in the infant/child as well as a dysfunctional caretaker-infant/child interaction.⁶ Confirmation of non-organic causes for FTT is based upon adequate growth and development after appropriate nutritional management of the case (see Management section). Frequently, children with medical conditions who present with FTT also concurrently have a number of environmental and psychosocial components to their problem. These cases are classified as FTT of "mixed etiology."

Children whose heights fall below the third percentile for age often get consideration for having FTT. As previously mentioned, only those children who have severe malnutrition or have been chronically malnourished are likely to have both weight and height below the third percentile. Thus, more likely diagnoses to consider in children whose heights fall below the third percentile are Familial Short Stature (FSS) and Constitutional Growth Delay (CGD), often classified as "factitious FTT."⁶ Familial short stature is diagnosed in children whose final height is consistent with parental heights. These children tend to readjust their growth percentile according to their genetic makeup before 3 years of age.⁶ After 3 years of age, these children grow at rates comparable to children of average height. A calculation of mid-parental heights, or MPH's, (expected height of the child based on parents' heights) may be helpful in making the diagnosis:

MPH male = (father's height + mother's height +
5 inches or 13 cm) / 2

MPH female = (father's height + mother's height -
5 inches or 13 cm) / 2

If parental heights are below the third percentile and the child's MPH is below the third percentile, one should strongly consider FSS as the primary diagnosis in the absence of organic illness. Children with constitutional growth delay are classically described as being "late bloomers" or "slow growers." These children exhibit deceleration of growth in the first 2 years of life due to a delay in skeletal maturation but then experience a growth spurt and catch up growth during adolescence. Notable in these patients is a significant weight deficit for length by the sixth month of life, which is not normally found in FSS. Table 1 highlights the differences between familial short stature and constitutional growth delay.

Table 1 Familial Short Stature vs. Constitutional Growth Delay	
Familial Short Stature bone age = chronological age no catch up growth normal weight for length family history of short parents/sibling	Constitutional Growth Delay bone age < chronological age catch up growth weight deficit for length 60-90% of family history of delayed growth and pubertal development
* Adapted from Maggioni and Lifshitz (1995). ⁶	

The organic causes of FTT fall under one of five major categories: (a) poor caloric intake; (b) poor food assimilation; (c) excessive loss of calories; (d) increased energy requirements; and (e) prenatal insults. The common thread among all five categories is an energy intake insufficient to meet the infant/child's needs.⁹ Non-organic failure to thrive is typically preceded by one or several of the following risk factors:

- a. *Temperament of the Child* — fussy, irritable, distractible and impatient child;¹⁰
- b. *Interaction between Mother and Child* — poor communication and encouragement, minimal positive enforcement during feedings;¹¹
- c. *Infantile Anorexia Syndrome* — food refusal or extreme food selectivity and undereating despite parents' efforts to increase the infant's food intake, driven by infant's thrust for autonomy;⁶
- d. *Psychosocial Environment* — stresses on parents, poverty, dysfunctional marital relationship;¹²
- e. *Parental Characteristics and Beliefs* — e.g. some parents may believe that limiting food during early childhood will develop into healthy eating habits in later life; or some parents who are overweight may feel the need to place their child on a diet; or vegans feeding their children inappropriate diets causing iron deficiency anemia, vitamin B12 deficiency or rickets.⁶

Table 2 illustrates some of the organic and non-organic causes of failure to thrive.

Approach to Diagnosis

The accurate diagnosis of the etiology in cases of FTT relies on four pertinent components: a) observation of the parent-child interaction; b) accurate and thorough history; c) complete physical examination; and d) laboratory investigation.

A. Observation of the Parent-Child Interaction

Ideally, observation of the parent-child interaction would take place during a feeding session in the home. This could be accomplished through videotape taken by the parents and brought into the doctor's office. Alternatively, parent-child dynamics can also be assessed by observing a feeding session in the doctor's office. Focus should be placed on the behaviour of both parties, and the responsiveness of each to the other's cues.

B. History

As an accurate and thorough history are important to the diagnosis of FTT, it is always best if both father and mother (and/or primary caregiver) are present during the interview. The complete history is composed of the following different segments:

i. Dietary History

Request parents to bring in a "food diary" of the past 3 to 7 days prior to visiting the physician's office. The food diary

should have records on the number of meals per day, amount and type of food consumed at each meal, and number/type of snacks and drinks per day. For infants, physicians should review formula preparation techniques with parents and/or address breast feeding issues (mother's fluid intake, milk supply, feeding technique, let-down reflex).¹ Particular attention should be paid to the amount of milk and fruit juice consumed as children who drink lots of fluid tend to be full at meal times and hence, eat less.

Table 2
Etiology of Failure to Thrive

Organic Causes

Poor Caloric Intake — cleft palate, choanal atresia, esophageal motility problems, anemia, hypotonia, lead toxicity, hypothyroidism

Poor Food Assimilation — malabsorption (cystic fibrosis, inflammatory bowel disease, milk allergy, celiac disease, pancreatic insufficiency, parasites), GI obstruction (pyloric stenosis, malrotation, intussusception), CNS problems (increased ICP, cerebral hemorrhage), metabolic problems (inborn errors of metabolism, storage disease, hypercalcemia)

Excessive Loss of Calories — chronic diarrhea, gastroesophageal reflux

Increased Energy Requirements — chronic systemic infection (UTI, tuberculosis, AIDS), malignancy, renal disease (RTA, diabetes insipidus), cyanotic congenital heart disease, hyperthyroidism, cerebral palsy, juvenile rheumatoid arthritis

Prenatal Causes — intrauterine infection, maternal smoking or malnutrition, fetal alcohol syndrome, fetal hydantoin syndrome, chromosomal disorders

Non-Organic Causes

economic deprivation (inability to afford adequate amount of food)

emotional deprivation

dysfunctional home environment

child neglect (failure to offer adequate calories)

child abuse

accidental (poor feeding technique, error in formula preparation, improper dietary beliefs, insufficient lactation in mother)

Adapted from Leung et al. (1993).²

ii. Feeding History

This section of the history should focus primarily on the behaviour of the child and parents during the feeding session, as well as the conditions of the surrounding environment. For example, the following questions should be answered: what is the setting of the feeding sessions?¹ (in front of TV? in room? distractions?); who is present during feeding sessions?¹ (entire family? child only?); when does the child eat? (set times? when they want?); and how do parents facilitate feeding? (force-feed? positive/negative reinforcement?).

iii. Birth and Pregnancy History

Asking pertinent questions about the birth and pregnancy can help to rule out prenatal causes of FTT. One should normally inquire about birth weight and age, method of delivery, perinatal infection, asphyxia, maternal infections, smoking, hypertension, alcohol abuse and drug abuse.

iv. Postpartum History

Asking the mother about the period immediately following delivery can give the physician a sense of the mother's attitude toward her child and motherhood. Specifically, one should ask about disappointment with the baby's sex, maternal depression (postpartum) and the strength of the support system.⁹

v. Medical History

Screening questions covering some of the illnesses which cause FTT of organic etiology are appropriate in this section. Also ask about previous hospitalizations, accidents, surgery, and medications.

vi. Family History

In addition to asking about medical or psychiatric conditions which run in the family, it is also useful to ask about parental heights so that mid-parental height can be calculated for the child.

vii. Social, Psychosocial and Behavioural History

Asking about developmental or behavioural problems with the child in the past/present is crucial (risk factor for non-organic FTT). Other topics which should be covered include socioeconomic status, stresses on family, participants in child care, emotional state of family members, and the parent's perception of food and illness.

C. Physical Examination

A complete physical examination of all systems is required to check for any of the organic causes of FTT. Weight, height, and head circumference should be measured and plotted on appropriate charts. Be aware that children under 2 years of age should have their length measured recumbent rather than standing, because standing height may be as much as 2 cm less than recumbent height.⁹ The degree of severity of malnutrition can also be estimated using the weights obtained. In 1956, Gomez described specific criteria for classifying the severity of malnutrition.¹³ These criteria are described in Table 3.

Table 3
Gomez Criteria for
Classifying Severity of Malnutrition

Percent Median Weight for Age	Grade of Malnutrition
weight 90-100% of ideal body weight	normal
weight 75-89% of ideal body weight	I mild
weight 60-74% of ideal body weight	II moderate
weight <60% of ideal body weight	III severe

Adapted from Gomez (1956).¹³

D. Laboratory Investigation

Laboratory investigations are not indicated without specific findings, suggesting organic etiology from history or physical examination. In a study performed by Sills (1978), only 1.4% of lab studies performed were of positive diagnostic assistance.¹⁴ Additionally, all lab studies performed without specific findings from history or physical examination were of no diagnostic value.¹⁴ Thus, lab tests should only be ordered to help confirm clinical suspicion ascertained from history and/or physical examination. Lab tests should also be considered in cases of suspected non-organic FTT which do not respond to nutritional and multidisciplinary management.

Management

Management of FTT depends partly upon the underlying etiology. FTT of organic etiology must first be managed by treating the underlying illness. Nutritional therapy and some components of a multidisciplinary program may be appropriate for organic FTT as well. Ideally, non-organic FTT is managed through nutritional therapy and several components of a multidisciplinary program are designed to intervene at the level identified to be the cause of the growth deficiency. Hospitalization is indicated only under specific conditions.

A. Nutritional Management

Specific goals of nutritional therapy have been clearly outlined by Maggioni and Lifshitz (1995).⁶ These include a) achieving ideal weight for height; b) achieving catch-up growth; c) restoring optimal body composition; and d) parental education about nutrition of children. In order to achieve catch-up growth, children with FTT require approximately 1.5 to 2 times more energy than a normal child and about double the amount of protein. Daily caloric intake for catch-up growth can be calculated using the following equation:¹⁵

$$\text{kcal/kg} = (120 \text{ kcal/kg} \times \text{median weight for current height}) / (\text{current weight in kg})$$

Infants' formulas may be modified by adding carbohydrates (glucose polymers), milk solids, medium chain triglycerides or corn oil and multivitamins (iron, zinc) to increase the caloric content and nutrition of their meals. Some guidelines which may help parents feed their children adequately are as follows:

- a. 3 meals a day with no less than 3 snacks a day;¹⁶
- b. consume foods from each of the four major food groups;
- c. encourage high calorie meals and frequent snacks as total calories is the principal determinant of recovery: see Table 4 for high caloric foods;
- d. eat within a relaxed, stress-free environment and use positive reinforcement;¹⁶
- e. offer solids first and limit juices to 4 to 8 oz/day (while still making sure that daily fluid intake is adequate), since excessive fluids tend to reduce the intake of higher calorie solid foods.¹

Table 4
High Calorie Food Supplements

non fat dry milk	25 kcal/tbsp
cheese	100 kcal/oz
sour cream	30 kcal/tbsp
whipping cream	60 kcal/tbsp
butter, margarine, oil	40 kcal/tbsp
peanut butter	100 kcal/tbsp
instant breakfast	130 kcal/packet

Adapted from Bithoney et al. (1992).¹

B. Multidisciplinary Program

The utilization of a multidisciplinary program in the management of FTT underlines the complexity of the problem at hand. The more complex the case is, the more professionals should be involved. For example, cases of FTT of strictly organic etiology will not require behavioural intervention from a clinical psychologist, but will instead require more medical support from physicians and nurses. On the other hand, cases of FTT of mixed or non-organic etiology will require support from a number of different professions which may include health visitors (for home intervention), a clinical psychologist (for behavioural intervention), a dietitian (for nutritional management), a consultant pediatrician and nurse (for medical support), and possibly social work and child protection services for more severe cases involving dysfunctional families.¹⁷

i. Home Intervention

In a study done by Black *et al.* (1995), home intervention pro-

grams were designed to provide maternal support and to encourage parenting, child development and the use of informal and formal resources to help cope with the situation¹⁸. As non-organic failure to thrive is often rooted in psychosocial or family problems, family focused home intervention seems ideal in promoting healthy and productive living conditions for all family members. Black *et al.* (1995) discovered that children in the home intervention program scored better in areas of receptive language, and parents in the home intervention program tended to create more child-oriented home environments compared to controls.¹⁸

ii. Dietitian

The role of the dietitian is not only to recommend the appropriate diet for the child, but also to educate parents regarding catch up growth, nutrition and caloric intake, as well as addressing the dietary beliefs of parents.

iii. Pediatrician and Nurse

The medical team functions to ensure accurate assessment and follow-up of the child's weight and height as well as performing developmental screens in children suspected of suffering from developmental delay secondary to growth deficiency.

iv. Clinical Psychologist

The child psychologist often plays a critical role in behavioural modification and counselling of children who suffer from non-organic FTT.

v. Social Work and Child Protection Services

Only in the most serious cases are these parties involved in the management of FTT. They function to assess the child and family's functioning and to identify the problems in the home.

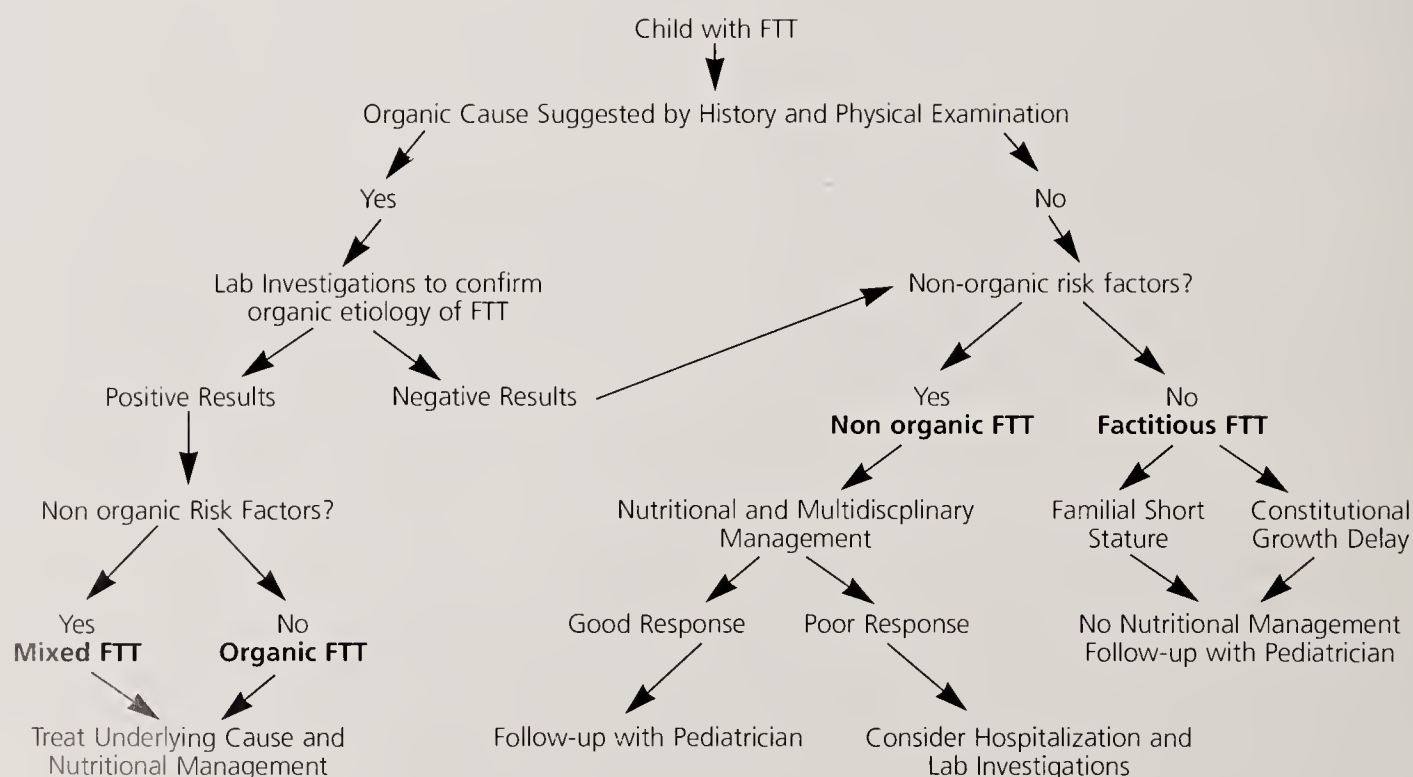


FIGURE 1. Approach to Diagnosis and Management of FTT

Initially, lab investigations are ordered only to confirm clinical suspicion of organic etiology, and not to screen for organic causes. The absence of findings on history and physical, and the absence of non-organic risk factors suggests factitious FTT. Appreciate the importance of nutritional and multidisciplinary management of FTT, particularly in cases of non-organic etiology.

Social workers offer solutions and guide parents towards community resources. Child protection services may become involved in cases where abuse or neglect is suspected and if the child is at risk of harm.⁷

C. Hospitalization

Ideally, FTT should be managed on an outpatient basis in a setting familiar to both the family and the patient. This way, intervention can focus on changing the habits and behaviours that cause many cases of non-organic FTT in the community. Hospitalization should be considered only under the following circumstances: 1) poor response to outpatient nutritional management; 2) extremely severe malnutrition (Table 3); 3) suspected parental abuse or neglect; and 4) presence of significant medical problems.⁶

Figure 1 is a flow diagram illustrating an approach to FTT based on the principles of diagnosis and management discussed above.

Follow-Up and Prognosis

During the follow-up period the child may begin to show symptoms of "Nutritional Recovery Syndrome." This syndrome is characterized by sweatiness, hepatomegaly (due to increased glycogen deposition in the liver), widening of sutures (because brain growth is greater than the growth of the skull in infants) and fidgetiness and/or mild hyperactivity.⁴ It is important to be mindful that there are many complications associated with FTT, most of which are reversible with adequate nutritional support and treatment of underlying organic illness. Some of these complications include lead poisoning, iron and zinc deficiency, impaired immunity, malabsorption, maldigestion, renal tubular acidosis, and hypothalamic dysfunction (decreased growth hormone, thyroid hormone, and somatomedin C).¹

The prognosis and outcome for children with FTT depends on a variety of factors and thus varies from case to case. Chronic undernutrition of early onset or chronic medical conditions as a cause of FTT have been shown to result in long term growth decrements.¹ Oates *et al.* (1985) reported that children suffering from non-organic FTT admitted to the hospital were significantly delayed in language development, reading skills and verbal intelligence.¹⁹ Another study also demonstrated that 55% of FTT children had psychomotor developmental delay.²⁰ These studies seem to magnify the importance of early detection and appropriate intervention for cases of FTT as children with mild or moderate FTT tend to achieve near normal or normal growth status and development with early intervention.⁹

Summary

In assessing a child with failure to thrive, it is important for the physician to take a full history and physical examination for organic causes of FTT. Lab investigations should be ordered only with clinical suspicion of an underlying organic etiology suggested by history and physical examination. Non-organic risk factors should also be inquired about, as the presence of these suggests either non-organic FTT or mixed FTT (if organic etiology is also confirmed). Patients who do not have

non-organic risk factors and no organic etiology should be considered as having factitious FTT. Finally, management of the problem should be started immediately as early intervention helps to decrease the likelihood of developmental delay. Dietary management should be instituted in all cases of FTT and multidisciplinary management organized by the physician based on the underlying etiology of FTT and the availability of resources.

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Smoking and Cardiovascular Disease: Clinical Manifestations, Pathophysiology and Methods of Smoking Cessation

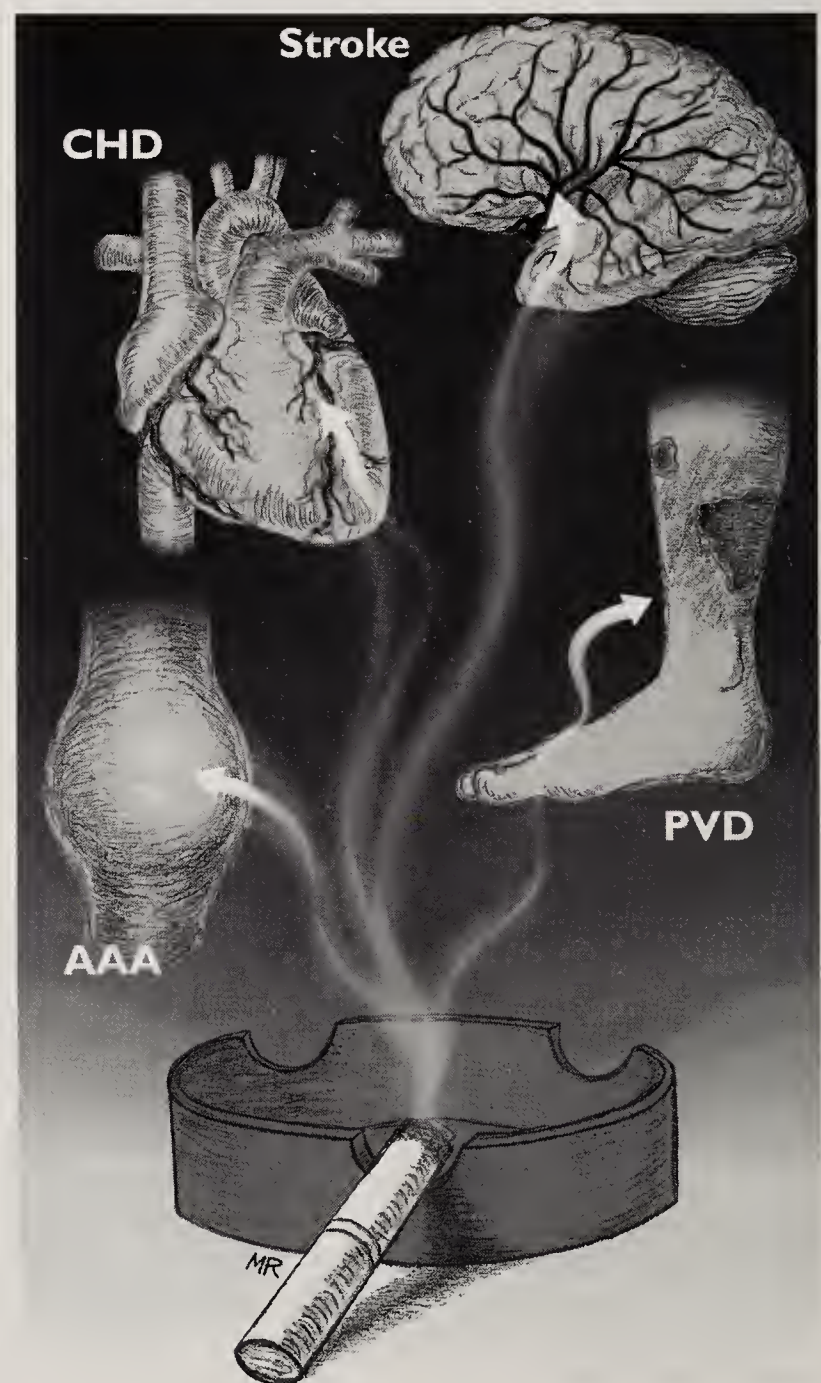
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Abstract

Both passive and active cigarette smoking are thought to increase the risk of cardiovascular disease, the leading cause of death in Canada.¹ The relationship between tobacco smoking and increased risk of coronary heart disease (myocardial infarction, vasospastic angina or sudden death), stroke (cerebral infarction, cerebral or subarachnoid haemorrhage), peripheral arterial disease, and aortic aneurysm has been well established in numerous longitudinal and cross-sectional studies.²⁻⁸ Smoking can elicit both acute and chronic vascular events due to the multiplicity of mechanisms involved: hematologic, neurohormonal, metabolic, hemodynamic, and molecular genetic pathways. Smoking cessation can result in both the inhibition and regression of pathophysiologic changes, decreasing morbidity and mortality amongst chronic smokers.

Introduction

Each year in Canada more than 16,000 cardiovascular deaths result from smoking, with many occurring prematurely before the age of 70. The overall prevalence of smoking has decreased for both men and women, yet this long term decline in smoking ended in 1993-94. The two demographic groups of particular concern are women and the young. Over the past 25 years, the prevalence of smoking amongst female smokers has dropped only 10%, while the prevalence amongst male smokers has dropped 30%. The rate of smoking amongst Canada's youth is on the rise: in 1990, 21% of



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males and females aged 15-19 were current smokers, but by 1994 the rates of current smoking increased to 26% and 29% for young men and women aged 15-19, respectively.⁹ Smoking not only affects those who actively smoke, but passive smoking has been implicated in causing cardiovascular disease among healthy non-smokers.¹⁰ This paper serves to review the epidemiology and pathophysiology of smoking-induced cardiovascular disease, and to highlight the importance of smoking cessation programs which view smoking addiction from both a biological and behavioural vantage point.

The Clinical Effects of Smoking

A. Coronary Heart Disease (CHD)

Smoking acts synergistically with two other major coronary heart disease (CHD) risk factors (hypertension and hyperlipidemia) to substantially increase the risk of CHD. Current smokers have a 70% increased risk of fatal CHD and a 2-4 fold higher risk of non-fatal CHD and sudden death compared to non-smokers.¹¹ Oral contraceptive use has a synergistic action with tobacco smoke to substantially increase the risk of myocardial infarction (MI) and stroke in women.¹² Population studies have demonstrated a two-fold higher risk of sudden death in male smokers without a prior history of CHD and a 6 fold higher risk in men with prior CHD, independent of other risk factors.¹³ Smoking can elicit angina pectoris at diminished cardiac workloads in those patients with limited cardiac reserve or coronary artery stenosis.¹⁴ In addition, the intended effects of anti-anginal medications are interfered with by concurrent smoking.

Cigarette smoking cessation substantially reduces the incidence of cardiac arrest, coronary death and MI, with improvements in heart rate, ischemia and lengthened symptom-free periods that essentially mirror the duration of smoke-free living.¹⁵ Former smokers display a large risk reduction in the first year after quitting, but may maintain a modestly-elevated CHD risk for many years (some up to 20 years) compared with those who never smoked. In those patients with a documented history of CHD, smoking cessation reduces risk rapidly to a level similar to the general population within a few years.¹⁵⁻¹⁹ Studies have shown that patients in the post-MI period have a 25-50% reduction in overall mortality and a reduced risk of recurrent infarction among smokers who quit.^{15,16,20,21}

As a group, cigarette smokers have been shown to exhibit lower survival rates, more frequent hospitalisations, more episodes of angina and impaired physical activity following coronary artery bypass graft surgery (CABG) as compared to non-smokers. Patients who continue to smoke after successful percutaneous coronary revascularization have a 44% greater risk of mortality and an increased incidence of Q-wave infarction.²²

B. Cerebrovascular Disease (CVD)

Cerebrovascular disease can be divided broadly into subarachnoid haemorrhage (SAH), intracerebral haemorrhage and cerebral infarction. It has been known for almost a decade that smoking causes stroke.²³ It has been estimated that almost one half of all strokes in the U.S. are due to

smoking, and the majority are of the ischemic type.¹⁵ Meta-analysis has shown that the overall risk of stroke associated with smoking was 1.5, but was differentiated by the type of stroke (Table 1). With haemorrhagic stroke, the risk associated with smoking increases linearly with the number of cigarettes smoked.²⁴⁻²⁶ The risk of stroke increases with age and is slightly greater for women versus men (relative risk (RR) 1.72 and 1.43, respectively) and the risk of SAH is increased in those women who smoke and use oral contraceptives concurrently.¹⁵

Smoking cessation can reduce the risks associated with stroke at any level of smoking. The longest follow-up study (26 years) has revealed that following smoking cessation, the risk among smokers is substantially reduced within 2 years and is at the level of the general population within 5 years.⁸

Table 1
The Relative Risk of Acquired Stroke
with Active Smoking

• Overall Risk	1.5
• Cerebral Infarction	1.9
• Cerebral Hemorrhage	0.7
• Subarachnoid Hemorrhage	2.9

Following smoking cessation, the risk of stroke drops in the first 2 years and is at the level of the general population within 5 years.

C. Peripheral Vascular Disease (PVD)

Smoking is the strongest risk factor associated with the development of peripheral vascular disease (PVD). As with CHD and CVD, smoking acts synergistically with the other risk factors increasing the risk associated for developing PVD.²⁷⁻²⁹ Those patients diagnosed with PVD who continue to smoke are at higher risk for early amputation, decreased rates of limb salvage with bypass surgery, and decreased patency of vascular grafts leading to unfavourable long-term outcomes when compared to non- and former smokers.²⁹⁻³⁵

All of the above effects are essentially reduced or reversed by complete or partial abstinence from cigarette smoking. Former smokers have approximately half the risk of claudication and PVD as current smokers.¹⁵ Following peripheral vascular surgery, those patients who quit smoking have a 2-fold improvement in long-term survival when compared to those who continue to smoke.³⁶ Patients who smoke less than 15 cigarettes a day (or have never smoked) have a 2-fold better success rate following arterial reconstruction than those who continue to smoke.³⁷

D. Abdominal Aortic Aneurysm (AAA)

There are many causes of abdominal aortic aneurysms (AAA) but the most common is atherosclerotic change in the endothelial wall of the affected vessel. Smoking is an important risk factor for the growth, subsequent rupture of AAA, and mortality following rupture independent of aneurysm

size.^{7,38} The risk of death following AAA rupture in those who quit smoking is 2-3 times the risk associated with those who have never smoked, but is still 50% less than in current smokers.^{15,39}

Tobacco-Mediated Pathophysiology of CVD

A network of pathophysiologic mechanisms initiated by the toxic compounds found in smoke are responsible for acute and chronic vascular events. The distinction between acute and chronic vascular events can be difficult to discern which is due to the multiplicity of mechanisms involved: haematologic, neurohormonal, metabolic, haemodynamic, and molecular genetic pathways.

Mechanisms Associated with Acute Vascular Events Precipitated by Tobacco Smoke

Acute vascular events that can be attributed directly to cigarette smoking include: acute MI, sudden death, stroke, rethrombosis after thrombolysis, and restenosis following angioplasty.⁴⁰⁻⁴⁴

A. Haematologic Mechanisms (Table 2)

Cigarette smoke-mediated thrombosis is likely the final common step that precipitates acute MI and strokes. Cigarette smoking increases the risk of acute MI and sudden death to a greater extent than it increases the risk of angina. This may reflect the fact that angina is precipitated mostly by haemodynamic factors whereas sudden coronary death is mostly due to thrombosis of a ruptured atherosclerotic plaque which may be due to the activity of platelets.⁴⁵⁻⁴⁷ The observation that smokers who continue to smoke after thrombolysis or angioplasty have increased risk of reinfarction or reocclusion supports that thrombosis is a major mechanism of acute smoke-related events. Smoking just two cigarettes alone causes a 100 fold increase in platelet adherence,⁴⁸ while the enzyme cyclooxygenase is inhibited both acutely and chronically by cigarette smoke leading to prostacyclin inhibition and thromboxane biosynthesis.⁴⁹ As a result, there is increased risk of uninhibited platelet aggregation since prostacyclin is a potent inhibitor of platelet aggregation while thromboxane is a platelet agonist and coronary vasoconstrictor.⁵⁰

Table 2 Acute and Chronic Haematologic Effects of Cigarette Smoking		
Acute	Chronic	Both
*↑Thrombus formation	↑Fibrinogen levels	*↓Plasminogen levels
↑Platelet activation	↑Factor VII levels	↑Thromboxane synthesis
↑RBC & WBC mass	↑SMC proliferation	↑Prostacyclin inhibition
	↑Polycythemia	↓Oxygenated hemoglobin levels
Note: *↑ Denotes "increases with smoking." *↓ Denotes "decreases with smoking."		

B. Neurohormonal Mechanisms

Nicotine acts presynaptically leading to norepinephrine, adrenocorticotrophic hormone, endorphin, prolactin and cortisol release.^{29,51,52} Stimulation of sympathetic ganglia results in increased peripheral resistance and blood pressure.⁵³ Ambulatory blood pressure monitoring reveals that long-term smoking increases heart rate and blood pressure throughout the day.^{54,55} Nicotine-mediated adrenal catecholamine release causes the increase in heart rate (positive chronotropic effect) while an increase in myocardial contractility (positive inotropic effect) is probably due to sympathetic innervation.^{29,53} The acute increase in catecholamines following smoking impairs increased coronary blood flow from constriction of epicardial and resistance blood vessels. Increased myocardial contractility coupled with heightened coronary and peripheral vascular resistance increases the myocardial oxygen demand which can lead to ischemia.

Tobacco smoke contains carbon monoxide (CO), which has a strong avidity for haemoglobin, thus lowering the oxygen-carrying capacity of the blood.⁵⁶ This effectively limits the availability of oxygen for myocardial metabolism which is superimposed on a background of increased demand on myocardial perfusion. Therefore, smoking can create a situation in which myocardial work is elevated on the background of diminished coronary perfusion and could lead to an ischemic event. Premature ventricular beats are increased after cigarette smoking and this is thought to be partially mediated by catecholamines, thereby increasing the risk of sudden death during an MI.²⁹ It has been speculated that CO may also play a role in lowering ventricular fibrillation thresholds in smokers.^{57,58}

Mechanisms of Chronic (Atherosclerotic) Vascular Events Precipitated by Tobacco Smoke

Atheroma formation is the hallmark of atherogenesis leading to chronic vascular disease which includes CHD, PVD, CVD and atherosclerotic aneurysm.

The chronic effects of smoking on platelets include the induction of smooth muscle cell proliferation from factors released from platelets, thus stimulating the migration of myocytes into the intima of blood vessels, eventually leading to chronic atherosclerotic damage.⁵⁹ Cigarette smoke also increases plasma viscosity, increases the levels of fibrinogen and Factor VII, while reducing plasminogen. White and red blood cell (RBC) mass values increase after smoking due to CO which reduces the oxygen-carrying capacity of RBCs and is accompanied by impaired red cell deformability. This leads to reduced thrombolysis, increased plasma viscosity and thus increased risk of thrombus formation.^{60,61} Chronic hypoxemia from CO exposure in the cigarette coupled with pulmonary pathology can lead to polycythemia, increasing viscosity with limiting coronary blood flow.

The levels of fibrinogen and increased plasma viscosity may persist for up to a decade after smoking cessation.⁶² In contrast, the number of red blood cells drop rapidly after successful abstinence from smoking.⁶² Fibrinogen may also contribute to atherosclerosis by activation of specific platelet receptors.⁶³

A. Metabolic Mechanisms

i. Lipid Abnormalities

Smoking-induced changes include, changes in serum lipid concentrations and enhanced peroxidation of LDL. Oxidised LDL is taken up by macrophages which transform into foam cells, the core of the atherosclerotic plaque. Smoking reduces HDL cholesterol (HDL-2) and may promote a change in HDL conformation, thus inhibiting its anti-atherogenic potential.^{15,64} Levels of LDL, VLDL and triglycerides are higher in smokers by interference via lipoprotein lipase activation.⁶⁵⁻⁶⁷ Nicotine causes the release of catecholamines, which in turn promotes lipolysis and release of free fatty acids. Fatty acids can then be turned into VLDL by the liver.⁷⁰ HDL levels increase by 6-8 mg/dL after smoking cessation.^{68,69}

ii. Endothelial Damage

Endothelial damage is a precursor to atherosclerotic development *in vitro* and is defined by swelling, contraction and bleb formation with resultant subendothelial edema. The endothelial damage may be due to multiple components of tobacco smoke, as oxidant and direct nicotine-induced damage of endothelial cells has been displayed.⁷¹⁻⁷³ Exposure to tobacco smoke either active or passive, has been shown to result in impaired, endothelium-dependent arterial dilatation due to impaired NO secretion from the damaged endothelium.⁷⁴⁻⁷⁷ Impaired release of NO in smokers results in the loss of coronary vasodilatation, inhibition of platelet aggregation, smooth muscle proliferation and adherence of monocytes to the endothelium. This scenario sets up an environment conducive to atheroma formation. Cigarette smokers have been shown to have elevated circulating neutrophil counts.⁷⁸ Neutrophils may contribute to endothelial damage by the release of oxygen-derived free radicals, leukotrienes and proteases.⁷⁹ These neutrophil-derived factors can also lead to platelet aggregation and activation.

B. Molecular Genetic Mechanisms

Research has shown that smooth muscle cell (SMC) apoptosis (programmed cell death) occurs within the intimal layer of an atherosclerotic plaque.^{80,81} Aortic aneurysm SMC density is significantly decreased in the media layer, with increased p53 production and accumulation as compared to normal and aorto-occlusive patients.⁸² Therefore, apoptosis may play a role in both atherosclerotic and AAA degenerative disease by limiting the growth of SMC in different layers of the vascular wall.

Effects of Smoking Cessation on the Pathophysiology of Cardiovascular Diseases

Mechanisms such as altered platelet function, vasospasms, elevated neutrophil counts and reduced oxygen-carrying capacity of the blood are rapidly reversible following smoking cessation. In contrast, the development of atherosclerotic plaques are inhibited with smoking cessation but the process itself is minimally reversible.⁷⁵

Smoking Cessation

Chronic self-administration of nicotine in the form of cigarette smoke is associated with neural adaptations leading to the

development of tolerance and sensitisation. Recurrent cravings and withdrawal symptoms are prevalent following abstinence from smoking. Diagnostic criteria for nicotine withdrawal, according to the DSM-IV, include at least 4 of the following signs within 24 hours of abrupt cessation of nicotine use: dysphoria or depressed mood, insomnia, irritability/frustration/anger, anxiety, difficulty concentrating, restlessness, decreased heart rate, increased appetite, or weight gain.⁸³ Relapse from smoking cessation is due to both nicotine withdrawal plus social and psychological stresses.⁸⁴ Therefore, successful smoking cessation programs must address both the pharmacological and behavioural aspects.

Nicotine Replacement Therapy (NRT)

Nicotine replacement systems in the form of gum (nicotine polacriflex), patch (transdermal nicotine) and nasal spray have been approved for use in Canada. The cardiovascular risks of NRT for smokers, even those with underlying cardiovascular disease, are very small. The main role for NRT is to reduce the undesirable effects of nicotine withdrawal, particularly within the first two weeks of cessation. This enables the smoker to focus their attention on behavioural modification. The combination of cognitive-behavioural therapy with NRT is two to three times as effective as either intervention alone.⁸⁵ There are numerous styles of cognitive behavioural therapy as applied to smoking cessation and have been covered in other reviews.⁸⁶

Stages of Change

Not all patients suffering from smoking addiction improve with each program available. Part of the reason for treatment failure lies in the process through which smokers must pass on the way to smoking cessation. Patients modifying smoking habits move through a series of five stages: 1) *Pre-contemplation* – is the stage during which there is no intention to alter behaviour in the foreseeable future, and most of the patients in this group are unaware of their addiction. 2) *Contemplation* – includes those patients who believe they may have a smoking addiction but have not made a commitment to take action. 3) *Preparation* – is the stage during which the patient's intentions combine with behaviour. Patients in this stage are intending to take action in the next month and have unsuccessfully taken action in the preceding year. 4) *Action* – is the stage in which the patient modifies their behaviour, experiences, or environment in order to overcome their addiction. 5) *Maintenance* – is the stage during which people reinforce the gains made in the action stage and work to prevent relapse. These stages of change represent a temporal dimension that allows therapists to understand when particular shifts in attitudes, intentions and behaviour occur.⁸⁷ Meta-analysis reveals that the vast majority of patients are not in the action stage, with 10-15% of smokers prepared for action, approximately 30-40% in the contemplation stage and 50-60% in the pre-contemplation stage.⁸⁸ Most treatment programs are aimed at patients in the action stage and thus are ill-suited to the majority of smokers. This is a major reason for poor recruitment and retention rates in many smoking cessation programs. Therefore, it is important that the clinician and therapist recognise the stage of change of the patient, in order to apply proper treatment strategies.

Conclusions

There is a substantial and irrevocable body of evidence which shows that smoking is a major risk factor for all cardiovascular disease. Smoking continues to contribute to the mortality of both active and passive smokers in Canadian society. Tobacco smoke initiates a series of molecular pathways that ultimately manifest themselves clinically as CHD, PVD, CVD or AAA. This complex puzzle has been slowly pieced together through years of scientific research and no doubt will result in new treatments for cardiovascular disease. However, in the meantime, risk factor reduction is the best way of reducing the potential of developing cardiovascular disease in smokers. Proper recognition of the stage of change of the individual patient will increase the likelihood of successful smoking cessation.

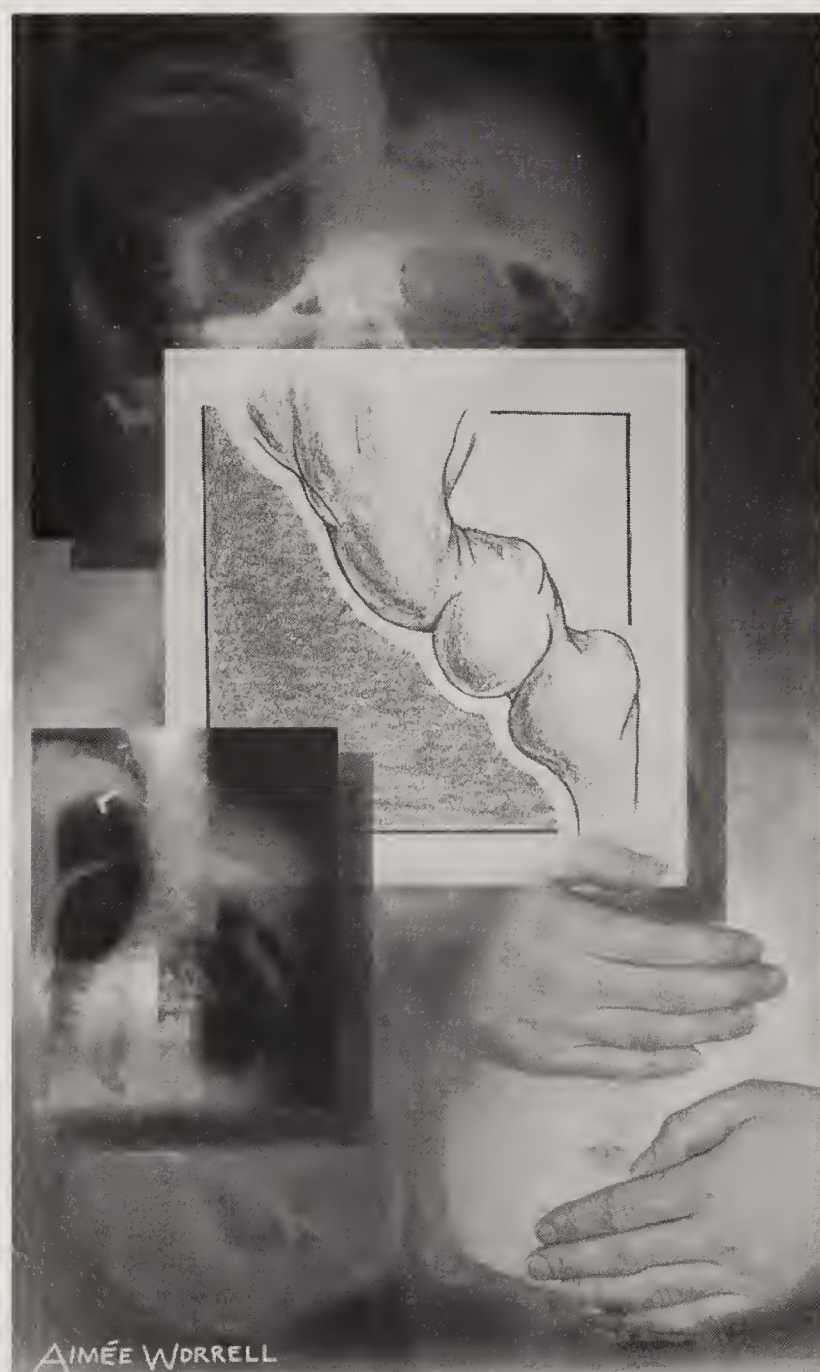
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Practical Aspects of the Abdominal Plain Film in Adults

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Abstract

When used appropriately, the abdominal plain film can provide the clinician with a wealth of useful information that can have a direct impact on patient management. In this article, we examine the clinical utility of the abdominal plain film, and present some common indications for ordering this study. Medical students and interns seem to have considerable difficulties in interpreting plain abdominal films. We will explore the reasons for this, as well as present a logical, systematic approach to interpretation. Finally, we will describe findings in two of the most common indications for ordering an abdominal plain film — bowel mechanical obstruction and adynamic ileus.

Introduction

When ordering imaging studies for patients, one can easily make the mistake of overlooking the plain abdominal x-ray in favour of more sophisticated and exciting imaging techniques, such as computed tomography (CT) scans, ultrasound, nuclear medicine, and magnetic resonance imaging. It is important not to underestimate the utility of the plain abdominal film. This relatively inexpensive study contains a wealth of information which, if interpreted correctly, can often make a major difference in the direction of patient management. In this article, we explore the indications for the plain abdominal film, as well as situations in which this study is not useful. In our experience, medical trainees have had considerable difficulty in interpreting the abdominal plain film. We will examine the reasons for this, as well as outline a logical, practical approach to the abdominal plain film. Finally, we will discuss two of the most common indications for abdominal plain films — mechanical obstruction and adynamic ileus. We have limited our discussion to adults, and have tried to emphasize the practical aspects of interpretation and use of this imaging modality.

Clinical Use of the Abdominal Plain Film

In a prospective study of abdominal radiographs in an emergency department, McCook *et al.* (1982) demonstrated that only 2% of abdominal plain films revealed any clinically useful positive findings.¹ Similarly, Eisenberg *et al.* (1983) reviewed 1,780 abdominal plain films, and found a significant abnormality in only 10%.² As a result, many have argued that the plain abdominal x-ray is an overused and inappropriate study in many cases.²⁻⁴ However, when used appropriately, the abdominal plain film provides a great deal of clinical utility. Specifically, when there is any question of bowel obstruction or ileus, perforated viscus, renal colic, peritonitis, mesenteric ischemia, or infarction, an abdominal plain film should be obtained.¹⁻⁵ Also, a plain abdominal film is an adequate study for the detection of foreign bodies (e.g. surgical sponges).

On the other hand, there are several situations where an abdominal film is not helpful, and may delay the patient from receiving definitive diagnostic studies or treatments. Table 1 summarizes the indications for abdominal plain films, as well as situations in which an abdominal plain film is not advised.

Types of Abdominal Plain Films

There are several different types of abdominal plain films. It is important for clinicians to familiarize themselves with the technique, indications, and limitations of each type of film in order to allow accurate interpretation of the films and avoid inappropriate ordering of films. The type of plain film examination ordered should be tailored to the patient and situation at hand.

A. The "Flat Plate"

This is what many clinicians mean when they talk about a "plain film" of the abdomen. It is an anteroposterior (AP or frontal view) supine film covering the area from the apex of the diaphragm to the obturator foramina. Often two films are required to cover this area. The flat plate is satisfactory for detecting foreign bodies and most intra-abdominal calcifications (e.g. ureteral stones). However, the clinician should avoid its routine use in patients with acute abdomen, because of the lack of upright views and poor visualization of the diaphragm.⁴

B. Upright and Left Lateral Decubitus Films

The upright film is an AP view, taken with the patient standing or sitting up. It is used for two reasons: 1) to identify the presence of free intraperitoneal air (pneumoperitoneum); and 2) to detect the presence of intestinal air-fluid levels. In patients who are unable to stand or sit, the left lateral decubitus (LLD) film serves the same purpose as the upright film. It has been argued that the LLD film is more sensitive for detecting pneumoperitoneum than the upright abdominal, while still less sensitive than the upright chest film.⁴

C. The Abdominal Series

This series of films is also known in different centres as "three views of the abdomen" or the "obstruction-perforation series." Three films are taken - a supine, an upright, and a LLD. Often a posteroanterior (PA) upright chest film is also included in this series, in order to detect the chest pathology (e.g. pneumonia, effusion, rib fracture, diaphragmatic hernia) that may cause the patient's abdominal symptoms. The upright chest film is also

superior to the upright abdominal film in detecting free pneumoperitoneum (this has to do with the obliquity of the x-ray beam in the upright abdominal film). See Figure 1 for an example of a large pneumoperitoneum. In fact, some suggest that the upright film may be an unnecessary study in the abdominal series.⁶⁻⁸ Mirvis *et al.* (1986) reviewed 252 patients evaluated for acute abdominal pain with a PA chest, supine abdominal, and upright abdominal films.⁹ They concluded that the upright abdominal film added very little, if any, diagnostic information and could be eliminated to reduce cost, time, and radiation exposure without loss of diagnostic accuracy.

Table 1
Indications for Abdominal Plain Films

Strong Indications
• perforated viscus
• bowel obstruction/ileus
• renal colic
• mesenteric ischemia
• other (infrequent, but potentially life-threatening and plain films may be pathognomonic):
• volvulus
• emphysematous cholecystitis
• toxic megacolon
Debatable Indications
• sepsis
• trauma
Inappropriate Indications
• gastrointestinal bleeding
• uncomplicated biliary disease
• acute pancreatitis
• ascites

D. Others

There are two other types of abdominal plain films which are rarely used today. The first is the right lateral decubitus film. This film is not useful in detecting pneumoperitoneum, because it does not offer new information over a LLD, and should not be included in the routine abdominal series.⁴ The second is the supine cross-table lateral film. With the patient lying supine, the x-ray beam is directed laterally through the patient's abdomen. It has been used in the past as a quick screen to assess the size of a calcified abdominal aortic aneurysm or to confirm an incarcerated ventral hernia. It is inadequate in detecting pneumoperitoneum or the location of air-fluid levels.

Approach to Reading an Abdominal Plain Film

A. Difficulties with Interpretation

In our opinion, most medical students and interns do not have the same level of confidence they have with chest x-ray interpretation. First of all, normal anatomy simply shows up better on chest x-rays than on abdominal films. In the thorax, differ-

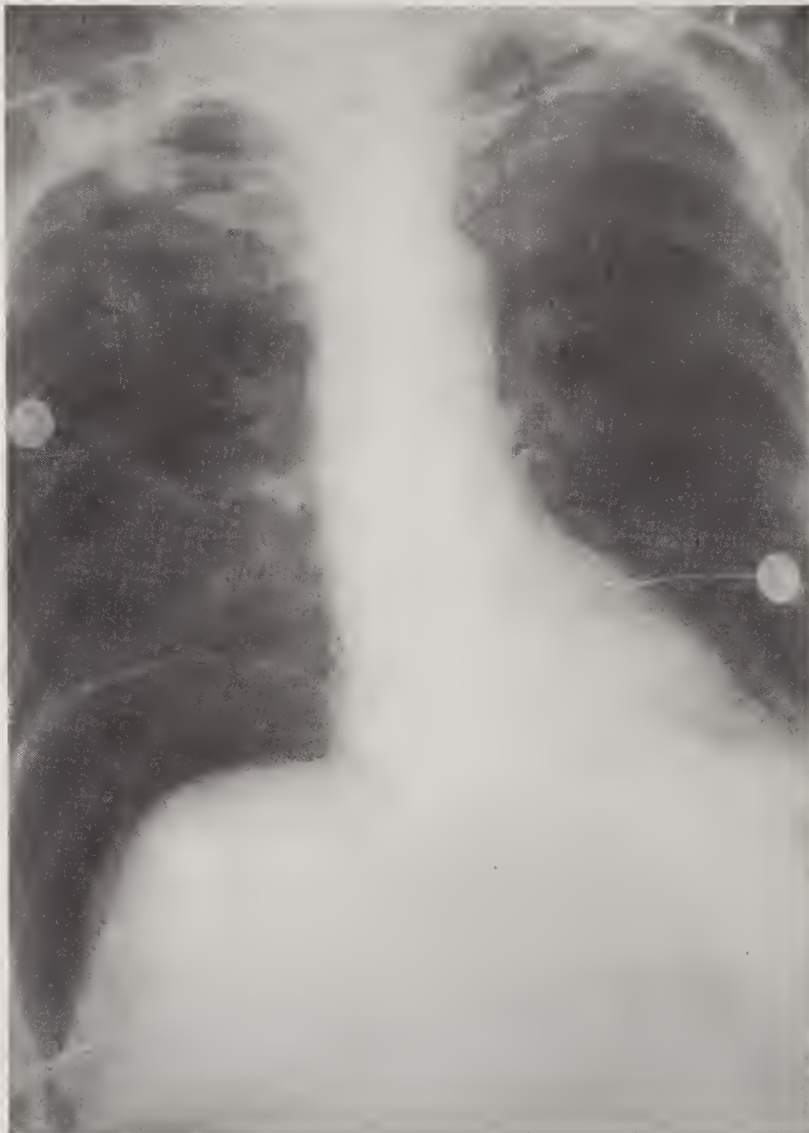


FIGURE 1. Large Pneumoperitoneum. Chest film demonstrating a large pneumoperitoneum in a patient with a perforated abdominal viscus.

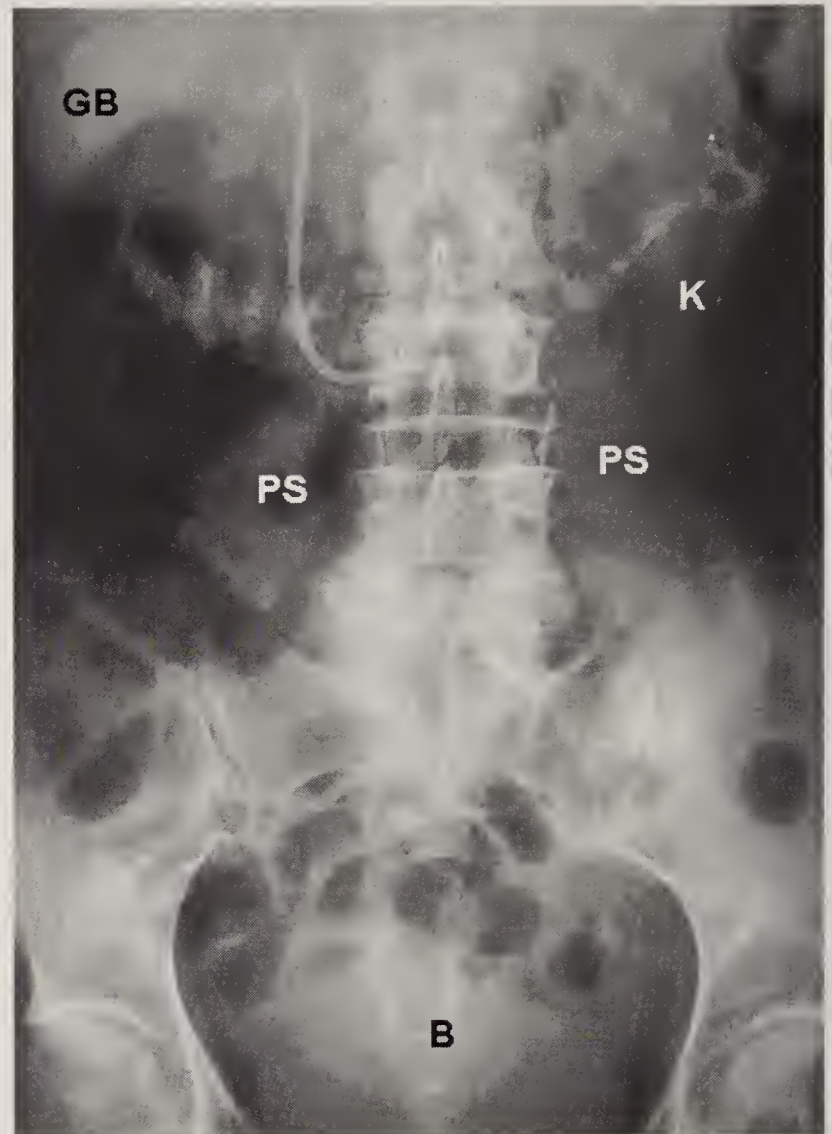


FIGURE 2. Normal Anatomy. Supine view of normal anatomy. Note the psoas muscles (PS), gallbladder (GB, opacified from a previous contrast study), lower pole of left kidney (K), bladder (B), gas pattern (contrast from previous study), and calcifications.

ent anatomical structures have widely different radiodensities (e.g. air in the lungs vs. heart muscle) that provide readily visible margins and profiles that aid immensely in anatomical recognition. In contrast, the various organs of the abdomen all have very similar soft tissue radiodensity. As a result, anatomical borders are not as apparent, and everything seems to blend into a confluent grayish shadow. Without aerated lungs to outline anatomical boundaries for us, we are forced to rely on the layers of fat that outline some organs (e.g. kidneys) and the air that normally lies in the bowels. Secondly, the normal intestinal air pattern is extremely variable, making it difficult for students to establish a baseline sense of normal in their own minds. It takes much longer to establish just what is normal in the abdomen, and often students simply have not seen enough films.

B. Systematic Study of the Abdominal Plain Film

Just like reading a chest x-ray, a systematic approach is the key to accurate and confident interpretation of the abdominal plain film. Table 2 gives an example of a checklist approach to interpretation of the abdominal plain film. Figure 2 demonstrates much of the normal anatomy.

i. Identification

Begin by checking the name and age of the patient, as well as the date of the study. Make sure you are looking at the correct

film! Check what type of study you are looking at, often indicated in marker by the technologist.

ii. Supraphrenic Structures

Take a quick look at the lung bases and heart above the diaphragm, looking for any effusions, consolidation, rib fractures, or anything else that could account for your patient's symptoms.

iii. Bones

Inspect the lower thoracic spine and lumbosacral vertebrae, looking for any lytic or sclerotic lesions, as well as degenerative changes. Continue by inspecting the pelvis and the hips.

iv. Soft Tissues

Look for the peritoneal flank or fat stripe, usually seen outlining the margins of the abdomen lateral to the ascending and descending colon (see Figure 3). The flank stripe is not always seen, especially in thin elderly patients. It is often obliterated by intra-abdominal fluid (e.g. ascites, hemorrhage) and by inflammatory conditions of the abdomen (e.g. appendicitis, peritonitis).

Next, look for the psoas muscles which are nicely outlined by fat. The psoas margins can be seen adjacent to the lumbar spine, and they are pyramidal in shape with the apices located

superiorly. The psoas margin may be obscured in intra- or extraperitoneal inflammation, tumour, mass, or rupture of the abdominal aorta.

v. Solid Visceral Organs

Because of similar radiodensities, the various solid visceral organs may be difficult to see on the plain abdominal film. The outlines of the liver and spleen may be seen in the right and left upper quadrants, respectively. Hepatomegaly is often difficult to see on plain film, but sometimes may be seen as depression of the hepatic flexure. Splenomegaly is easier to detect, and may be seen as an indentation and/or displacement of the splenic flexure or gastric air bubble (see Figure 4). The kidneys are often visualized because they are outlined by perirenal fat. The left kidney is normally 1-2 cm higher than the right. The kidneys are usually 8-15 cm long (approximately the length of 3-4 lumbar vertebrae), with the renal hila at the level of L2 (right) and L1 (left) vertebrae, and the long axis parallel to the psoas margin. In the pelvis, look for the bladder and uterus contours. The gallbladder and pancreas are normally not visible, unless they contain calcifications (e.g. stones). Inspect for any abnormal calcifications or masses, or any changes in shape or size of any of the abdominal organs.

Table 2
Checklist for Interpretation of
Abdominal Plain Films

Identification	• type of study – e.g. flat plate, upright, LLD • name and age of patient • date and time of study
Supraphrenic Structures	• lung bases • heart
Bones	• vertebrae and lower ribs • pelvis and hips
Soft Tissues	• flank stripe • psoas muscles
Solid Visceral Organs	• liver • spleen • kidneys • gallbladder and pancreas – normally not seen • bladder, uterus • abnormal masses
Gas Pattern	• intestinal gas pattern – dilatation, air-fluid levels, mucosal thickening • extraintestinal gas pattern – pneumoperitoneum, pneumobilia, hepatic portal venous gas, abscess, intramural gas
Calcifications	• gallstones, renal stones, fecaliths, appendicolith, phleboliths • pancreatic calcifications

vi. Gas Pattern

The next step is to inspect the gas pattern, both intra- and extraintestinal. Normal and abnormal intraintestinal gas pattern will be discussed later.

vii. Calcifications

Note any intra-abdominal calcifications.

C. Normal Intestinal Gas Pattern

One of the most difficult tasks in learning how to interpret the abdominal x-ray, is getting a sense of the normal gas pattern in the gut. This pattern is extremely variable from patient to patient, and even within the same patient over time.

i. Distribution

Normally, there are small amounts of gas in the stomach and throughout the colon. Gas in the stomach is seen as a gas-fluid level in upright films, or a round collection in the body of the stomach on supine films. Proximally, large bowel gas tends to be round to square shaped, divided by 3-4 mm haustral indentations. Distal large bowel gas appears as sausage-shaped collections. Depending on the amount of air, the rectum may appear diamond-shaped (little air) to circular (lots of air).¹⁰ Classically, we are taught that the small bowel contains little or no air. However in reality, the amount of air in the small bowel is extremely variable and depends on the degree of aerophagia in a given patient.

ii. Caliber

The caliber of the small bowel is normally 2.5-3.0 cm. The colon is larger more proximally than distally, and is normally 5 cm in the ascending colon, 4 cm in the transverse, and 3 cm in the descending colon.

iii. Gas-Fluid Levels

Gas-fluid levels are normally seen in the gastric fundus on upright films, and occasionally in the first part of the duodenum or in the right colon.

iv. Mucosal Lining

The small bowel is lined by the valvulae conniventes, which may be seen all the way through the lumen. The large bowel is lined by haustra which only partially cross the lumen. Table 3 demonstrates some of the essential differences between small and large bowel on radiograph.

Common Abnormal Findings

The abnormalities that may be seen on abdominal plain film can be categorized into abnormal gas patterns (intestinal and extraintestinal), soft tissue abnormalities, and calcifications. In this paper, we have chosen to focus on abnormal intestinal gas patterns.

A. Types of Abnormal Intestinal Gas Patterns

There are two major gas pattern abnormalities in the gut:

i. Distention or Dilatation of Bowel Loops

Small bowel dilatation greater than 3 cm or large bowel dilatation greater than 5 cm is usually abnormal.¹¹ A single air-filled loop of small bowel or colon that is distinctly much larger than

others on serial films may represent local dilatation. Multiple air-filled loops of bowel usually represent adynamic ileus or mechanical obstruction (small or large bowel).

ii. Presence of Gas-Fluid Levels

The presence of gas-fluid levels is not necessarily abnormal. Gammil and Nice (1992) reported that the average number of gas-fluid levels in a normal person (usually in the colon) is 3 to 5, typically less than 2.5 cm in length.¹² However, this varies greatly, and the significance of gas-fluid levels must be evaluated in the context of the clinical picture and the presence of other radiological abnormalities.

B. Adynamic Ileus

Often referred to as just “ileus,” this refers to an adynamic type of obstruction related to loss of peristaltic activity. As a result, the small bowel accumulates fluid and gas. The patient may complain of anorexia, nausea, abdominal discomfort, and possibly vomiting. On physical exam, one may find abdominal distention, diffuse tenderness, and absent or diminished bowel sounds. Adynamic ileus may be generalized or localized:

Table 3
Small Bowel vs. Large Bowel

	Small Bowel	Large Bowel
Mucosal lining	valvulae conniventes • completely across lumen • numerous • narrowly spaced	haustra • partially across lumen
Location	central	peripheral
Maximum diameter	2.5-3.0 cm	5 cm
Amount of gas	little or no air (extremely variable!)	usually some air
Wall thickness	2-3 mm	2-3 mm

i. Generalized Ileus

Generalized ileus may be caused by: post-operative state, peritonitis, hypokalemia, trauma, or peritoneal dialysis. Mild to moderate distention of both the large and small bowel is seen in a rather nonspecific pattern. In the colon, there may be a loss of the haustral pattern as the bowel dilates, and the right colon tends to get larger than the left.¹⁰ In addition, increased gas-fluid levels are usually seen. These occur in both the large and small bowel in an even distribution, and on upright films, these levels will be at the same height relative to the vertical axis.¹² Compared to mechanical obstruction, the affected segments tend to be longer.¹²

ii. Localized Ileus

A localized ileus is recognized by a single dilated loop that remains in the same location on several films. It may occur in

both the small and large bowel, and is usually adjacent to an area of inflammation. An example of this is the single “sentinel” loop “guarding” appendicitis in the right lower quadrant, pancreatitis in the mid-abdomen, or cholecystitis in the right upper quadrant.

C. Mechanical Obstruction

Classically, mechanical obstruction will give a radiographic appearance of bowel dilatation due to the accumulation of gas and fluid proximal to the point of obstruction. Distal to the point of obstruction, there is usually diminished bowel caliber with little or no gas and fluid as peristalsis moves bowel contents rectally.

In upright and decubitus films, gas-fluid levels are seen proximal to the obstruction. These are usually short segments of varying heights. Findings often vary over time, thus serial films may be extremely helpful.

i. Small Bowel Obstruction

The most common causes of small bowel obstruction are: 1) adhesions and fibrous bands from previous surgery, 2) incarcerated hernia, and 3) neoplasms.¹¹ Other causes include gallstone ileus, small bowel volvulus, and intussusception. The patient may complain of anorexia, nausea, vomiting, sharp or severe diffuse abdominal pain, initial diarrhea, or absence of flatus or bowel movement. On physical exam, one may find abdominal distention, tympani, increased and high-pitched bowel sounds, and diffuse tenderness.

The typical radiographic appearance of small bowel obstruction is 1) gaseous distention of multiple, centrally located loops to a

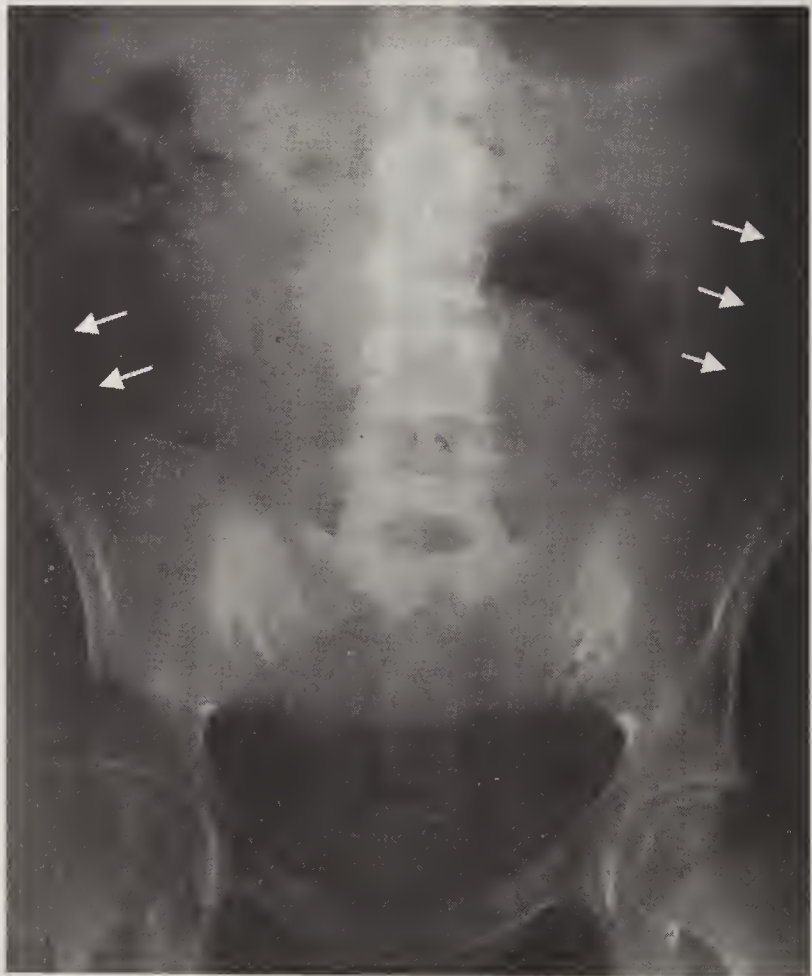


FIGURE 3. Arrows on supine view demonstrate properitoneal flank stripe.

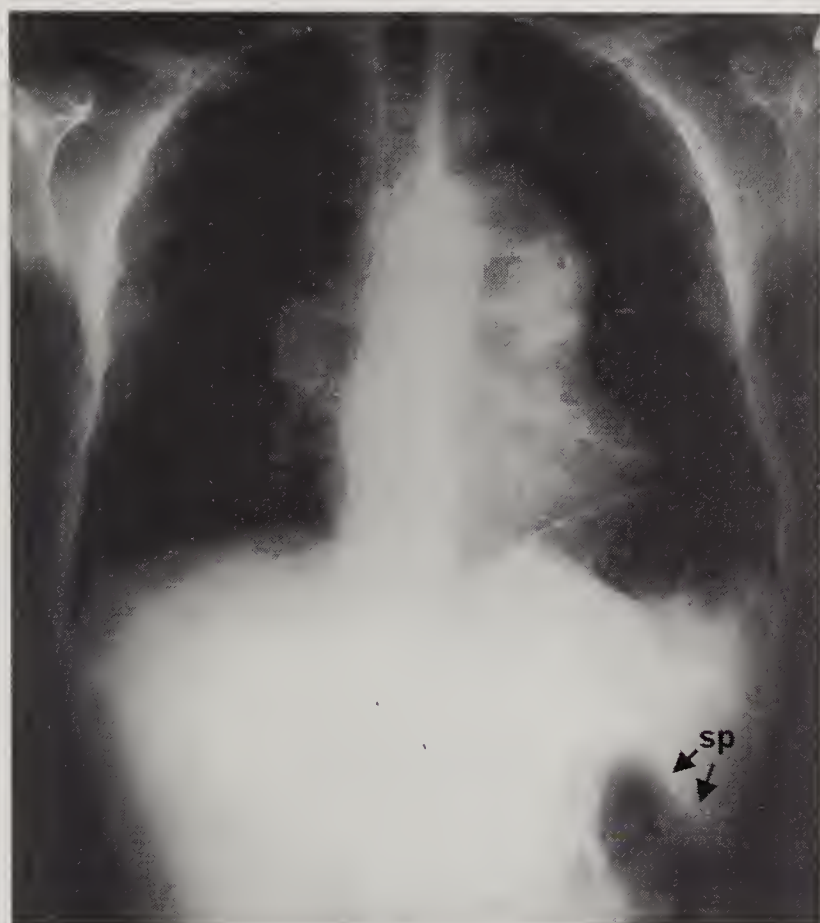


FIGURE 4. AP chest film showing splenomegaly.
Note the indentation of the splenic flexure by the enlarged spleen.

diameter of greater than 3 cm¹¹ and 2) short gas-fluid levels of varying heights on upright/LLD films (see Figures 5 and 6). Often a “step ladder” appearance is seen with the valvulae conniventes creating the “steps” across the dilated loops. In very early obstruction, there may still be gas seen distal to the point of obstruction, but eventually the distal bowel is cleared, and becomes completely gasless.

If only small amounts of gas are present in a predominantly fluid-filled bowel, the typical gaseous distention will not be seen. Instead, a row of small gas accumulations, tightly grouped together in a “string of beads” will be seen in the dilated valvulae conniventes. This “string of beads” sign is pathognomonic of small bowel obstruction.¹² Upper gastrointestinal contrast studies are not particularly useful in determining the level of obstruction due to dilution of the barium in large fluid collections proximal to the obstruction.

ii. Large Bowel Obstruction

In the large bowel, the most common causes of obstruction are: 1) colon carcinoma, 2) diverticulitis, and 3) volvulus.¹¹ The patient often gives a history of abdominal pain, obstipation, nausea, and distention. As in all mechanical obstructions, the typical findings are 1) proximal large bowel dilatation with little or no gas in the distal colon, and 2) short gas-fluid levels of varying heights. The degree of dilatation is greater than that seen in small bowel obstruction, with large bowel loops distending to greater than 5 cm.¹¹

Of special importance is the diameter of the dilated cecum. The cecum has a thinner and weaker wall than the rest of the colon, therefore the risk of perforation is much higher. The critical transverse diameter beyond which there is a greatly

increased risk of cecal perforation has been reported as 9 cm.¹³ At this point, acute decompression is recommended.

The presence of gas in the rectum does not rule out a low obstructing lesion. Gas may be introduced via digital rectal exam, colonoscopy, rectal temperature determination, and enemas.

In a large bowel obstruction, absence of gas in the small bowel depends on 1) how early the obstruction is, and 2) the competency of the ileocecal valve. In early large bowel obstruction, there will be little or no air in the small bowel, regardless of the competency of the ileocecal valve. In a late large bowel obstruction, distended loops of large bowel will decompress through an incompetent ileocecal valve (found in 50-90% of individuals),¹³ so that gas will be seen in a distended small bowel. If the valve is competent, the small bowel will become dilated due to a secondary mechanical obstruction at the valve.

It is often difficult to distinguish between large bowel obstruction and generalized adynamic ileus. Table 4 shows some of the key differences. Table 5 illustrates some of the differences between small bowel and large bowel obstruction. Contrast enema and colonoscopy are essential in ascertaining the cause of obstruction.

Table 4
Large Bowel Obstruction
vs.
Generalized Adynamic Ileus

	Adynamic Ileus	Large Bowel Obstruction
Gas-fluid levels	longer	shorter
Diameter of Dilated loops	normal or mild to moderate dilatation	usually dilated to greater diameter
Distribution	throughout small and large bowel	no gas distal to site of obstruction (unless very early)

Table 5
Small Bowel
vs.
Large Bowel Obstruction

	Small Bowel Obstruction	Large Bowel Obstruction
Frequency	more common (80%) ¹⁴	less common (20-30%) ¹⁵
Diameter	>3 cm	>5 cm
Number of loops	many	few
Location of loops	central	peripheral
Markings	valvulae conniventes	haustra



FIGURE 5. Supine View showing a Small Bowel Obstruction.
Note multiple dilated stacked loops of small bowel; their central location and transversing valvulae conniventes further suggest dilatation.



FIGURE 6. Left lateral decubitus film, of another patient with small bowel obstruction, shows multiple horizontal gas-fluid levels.

Conclusion

In this article, we have presented the plain abdominal film as a useful radiological study when utilized correctly. We have explored the clinical use, indications, and different types of abdominal plain films. A basic approach to interpretation was introduced. Finally, a discussion of findings in obstruction and adynamic ileus has been presented.

There is a wealth of other pathology that may be found on plain abdominal films that is beyond the scope of this article. There are several conditions which a good clinician should be able to recognize on plain abdominal film, since they can be surgical emergencies. These include pneumoperitoneum, bowel obstruction, pneumobilia, hepatic-portovenous gas, toxic megacolon, volvulus, and intramural gas. Whenever in doubt, it is important to consult a radiologist.

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Group A Streptococcal Pharyngitis: Making an Evidence-Based Diagnosis of Acute Sore Throat

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Abstract

Acute sore throat represents one of the most common problems seen by general practitioners. The most important aspect of the diagnosis is establishing the presence or absence of Group A Streptococcal infection. Traditionally, a variety of clinical signs and symptoms, as well as laboratory tests have been used. A recent “score card” from the Institute of Clinical Evaluative Sciences (ICES) attempts to define a rational approach to making the diagnosis based on the presence or absence of four specific clinical findings. This “score card” constitutes a clinical test to which probabilities of disease are assigned for each level of test result (number of findings present). The appropriate management strategy is then recommended based on the “score card” result. Although a valuable contribution, this algorithm’s limitations include the lack of a true gold standard and the use of positive predictive values, which are contingent on the pre-test probability of disease, to report test characteristics. Future research might be directed at prospectively determining likelihood ratios for each level of the “score card.” This would allow for the determination of post-test probability for any pre-test probability. In addition, consideration might be given to the use of the rapid streptococcus test in place of throat swab and culture.

Introduction

Acute sore throat is amongst the most common symptoms for which patients visit their family physicians. An approach to acute sore throat raises important questions such as whether the patient has Group A Streptococcus (GAS) infection, whether empiric treatment is warranted, or whether additional tests should be performed. Given the

prevalence of acute pharyngitis, these decisions have significant clinical as well as cost implications.

The key diagnostic question in a patient presenting with pharyngitis is whether the infection is due to GAS.¹ GAS accounts for 5-40% of sore throats and can result in complications such as rheumatic fever, skin rash, otitis media, post-streptococcal glomerulonephritis and retropharyngeal and peritonsillar abscesses.¹ Rheumatic fever is the most serious complication of GAS pharyngitis. It carries the risk of developing rheumatic heart disease, which though rare, may prove to be fatal. With prompt diagnosis and early treatment of GAS pharyngitis, the incidence of rheumatic fever following GAS pharyngitis has been reduced to 3%.² On the other hand, it is important to differentiate between viral and bacterial infection to prevent the unnecessary use of antibiotics, and thus reduce the chances of bacterial resistance in those not suffering from GAS pharyngitis.³

There have been numerous recommendations in the literature for a rational approach to acute sore throat including a recently published algorithm from the Institute for Clinical Evaluative Sciences (ICES). This paper discusses the signs and symptoms of GAS pharyngitis and the available laboratory tests for its diagnosis. It also summarizes and critically reviews the ICES diagnostic approach and suggests directions for future research.

Diagnosis of GAS Pharyngitis

There are a number of modalities available to the physician to assist in the diagnosis of GAS pharyngitis. These include clinical assessment (signs and symptoms) and laboratory studies such as the throat swab and culture, rapid streptococcal antigen test, and determination of Anti-Streptolysin O (ASO) titres.

A. Clinical Assessment

Clinical assessment can be a very important modality in making the diagnosis of GAS pharyngitis.⁶ On history, symptoms suggestive of GAS pharyngitis include: pharyngeal pain of duration more than 24 hours but less than a week, temperature greater than 38.5°C, anterior cervical lymphadenopathy, and lack of cough. There are other less specific symptoms such as chills, myalgia, headache, nausea, and in children, emesis. On physical examination, a patient with GAS pharyngitis may present with pharyngeal erythema and exudate, petechiae of the palate, anterior cervical lymphadenopathy, and sandpaper rash on the trunk.

Although the clinical presentation of other types of pharyngitis may be similar to those of GAS, there are features that often differ. In infectious mononucleosis, for example, lymphadenopathy tends to be generalized and scleral icterus and possibly hepatosplenomegaly are present.⁶ On the other hand, viral pharyngitis has cough and coryza as the primary findings.⁶

B. Laboratory Studies

Although the clinical assessment may be a very useful modality in obtaining information, a laboratory test is often

necessary to confirm the provisional clinical diagnosis of GAS pharyngitis.

i. Throat Culture Test

Throat culture is considered to be the gold standard in detecting GAS infection. An adequate sample can be obtained on a dry swab under direct vision from the posterior pharynx and tonsils. This test is 90% sensitive under ideal conditions and is slightly less sensitive in the office setting. Its specificity is less than 100% because the test also detects carriers,⁶ i.e. hosts who do not exhibit active infection. In addition, one to two days are required to obtain the culture result, which may delay management decisions.

ii. Rapid Streptococcal Test

This test, which can be easily performed in the office setting, gives a result within 7-70 minutes and is therefore, the most time-efficient test.⁶ It detects a carbohydrate antigen specific to GAS obtained from the throat swab specimen through either latex particle agglutination or enzyme-immunoassay. The positive predictive value of the test under ideal conditions is 92% and in the office setting, approximately 86%.

iii. Anti-Streptolysin O Titres

The anti-streptolysin O (ASO) titre is a serological test that determines the level of antibodies produced in response to the streptolysin O antigen. It is highly sensitive in both the late acute and convalescent states of the infection. It also detects previous infection which is otherwise difficult to identify. However, it is not useful in detecting the infection in its early acute phase (<5 days), as the immune response to streptococcal antigen takes time to develop. The antibody titres decrease with time, allowing for retrospective determination of the approximate time of infection.

In current practice, a comprehensive clinical assessment and one or more laboratory tests are used to make the diagnosis of GAS pharyngitis. The ICES algorithm proposed by McIsaac *et al.* (1997) which rationally structures the diagnosis of GAS pharyngitis based on clinical features and test results, will now be discussed.^{3,4}

ICES Approach

The algorithm suggested by McIsaac *et al.* (1997) in the ICES "sore throat score" involves two steps in diagnostic testing.⁴ The first step is a clinical assessment of the patient's signs and symptoms derived from a study by Centor *et al.* (1981).⁷ This study identified four signs and symptoms as most predictive of GAS infection in patients with acute pharyngitis. These are fever greater than 38.5°C, exudate, cervical lymphadenopathy, and the absence of cough. The clinical assessment has five possible results, ranging from 0 to 4, depending on the number of signs and symptoms present.⁴

In Centor's original paper, each level of this test result was compared against the gold standard of throat swab and culture, and the probability of GAS pharyngitis was defined.

The ICES paper utilizes the concept of positive predictive values.⁴ The positive predictive value is the proportion of those with a particular test result who have the disease. It is calculated from a 2 X 2 table of sensitivity and specificity (see appendix).

Based on the positive predictive value associated with a particular test result, McIssac *et al.* (1997) advocate a management strategy that consists of either no action, culture with treatment dependent on culture results, or culture and empiric treatment.⁴ If the score is 0 or 1, the probability of GAS infection is less than 7%, and this is considered sufficiently low as not to warrant treatment or further investigation. If the score is 2 or 3, then the probability of GAS infection ranges from 8% to 34%. At this intermediate probability of disease, further investigation with throat culture is deemed appropriate and treatment is initiated based on culture results. If the score is 4, the probability of infection is 41-61%, sufficiently high to begin treatment without further testing. This cutoff incorporates data from a previous decision analysis which advocated empiric treatment at the post-test probability of greater than 50%.⁵ The algorithm is summarized in Table 1.

Table 1

ICES Algorithm

No. of Signs and Symptoms Present	Positive Predictive Value (%)	Action
0	2-3	No culture, no treatment
1	3-7	
2	8-16	Culture; treat if culture is positive
3	19-34	
4	41-61	Empiric treatment and culture

see Appendix for Definitions

Analysis

There are numerous issues that arise in a critical analysis of the ICES approach. First, the original paper used throat swab and culture as its gold standard to determine the positive predictive values associated with each level of the test result.⁴ Throat swab and culture detects both GAS infections and carriers. The carrier rate of GAS in the population may be as high as 15-20%.⁸ Therefore, throat swab and culture is likely to be less than 100% specific, and is thus an imperfect gold standard. Consequently, the validity of the positive predictive values derived from this paper must be interpreted with caution as they may over-estimate the true post-test probability of GAS infection.

Second, the properties of this clinical test are reported in terms of positive predictive values. For each level of the test

(i.e. number of signs and symptoms present), the probability of having the target disorder is given. However, positive predictive value, is contingent on the prevalence of disease in the population (i.e. pre-test probability). McIssac *et al.* (1997) report the clinical test characteristics based on an assumption of the prevalence of disease to be between 10% and 20%, representative of the average community.⁴ However, this may be a significant limitation in the applicability of this algorithm, since the prevalence of GAS pharyngitis varies seasonally and differs in different communities. It would not be possible to accurately use the ICES approach in any situation in which the pre-test probability was not 10-20%.

The solution to this problem is to determine likelihood ratios (see Appendix) for each test level. Likelihood ratios allow for the calculation of post-test probability from any pre-test probability using a nomogram. Unfortunately, neither McIssac *et al.* (1997) nor Centor *et al.* (1986) report a raw data table to allow for ascertainment of likelihood ratios.^{4,7} However, to illustrate the utility of this approach, the data in McIssac's paper has been used to reconstruct a raw data set (n=286 is derived from Centor's original paper). This data set is an approximation and is intended only as an example. It is reported in the Appendix.

Likelihood ratios can be calculated from raw data for each test level. For a given test result, the likelihood ratio contrasts the probability of that test result coming from someone with the target disorder as opposed to someone without the target disorder. The likelihood ratio calculation is explained in the appendix.

The likelihood ratio for each test results is shown in Table 2. Importantly, the likelihood ratio for 4 criteria would be considered diagnostic (>10). This confirms the current interpretation of the test result. Also, the likelihood ratios for 2 and 3 criteria are low (<5), confirming that these results do not contribute in a significant way to the diagnosis and that further testing is required. The likelihood ratio for 0 and 1 criteria are less than one, and decrease the probability of disease. These likelihood ratios are determined in a post-hoc analysis and without the original data set. They serve to illustrate the potential of this type of analysis and original research would be required to adequately calculate them.

Table 2

Likelihood Ratios for McIssac's Algorithm

No. of Signs and Symptoms	Likelihood Ratio
0	0.4
1	0.6
2	1.8
3	4.4
4	14.4

Several additional issues arise from analysis of this algorithm. Throat swab and culture are recommended as the

laboratory test to sort out those with an intermediate positive predictive value. The throat swab and culture may have a considerable false positive rate as discussed above. This would result in some unnecessary treatment.

Secondly, there may be some limitation due to the time delay involved in obtaining culture results (1-2 days). It is not known how soon an acute GAS pharyngitis should be treated to prevent rheumatic fever. However, the sooner treatment is initiated the better. Throat swab and culture will involve some delay in the decision-making process and a faster laboratory investigation, such as the rapid streptococcal antigen test, may be more appropriate.

Conclusion

There are a number of modalities available to the physician to assist in the diagnosis of GAS pharyngitis. These include clinical assessment of signs and symptoms and laboratory studies such as the throat swab and culture, rapid streptococcal antigen test, and determination of ASO titres.

The ICES algorithm is a rational approach to the diagnosis of GAS pharyngitis. In this approach, the pre-test probability is explicitly stated and clinical test properties are defined in terms of positive predictive value. This limits its use to a population with a particular pre-test probability. Given that clinically important variations in the prevalence of GAS infection occur, the dependence on pre-test probability may impair the utility of this clinical test. There is also a lack of a true gold standard for validation of clinical test characteristics. The throat swab and culture also identifies carrier states and is not 100% specific.

The ICES approach is easy to remember and straightforward to use. This is a strong advantage of this approach for busy family physicians. A possible improvement may be to substitute the rapid strep test for throat culture. The rapid streptococcus test is as valid as throat swab and culture. Because it is faster, it may be a more timely laboratory investigation for those with intermediate probability of disease.

Given the simplicity and strength of the ICES criteria, future studies should aim at evaluating this clinical strategy in a large population sample. Despite its limitations, the gold standard will likely have to be throat swab and culture. From data acquired in large populations, likelihood ratios with appropriate confidence limits could be determined for the different levels of the test. This will allow for a diagnostic tool that is independent of the pre-test probability, and hence will be applicable in any population setting. With a better evidence-based strategy defined by future research, family doctors will be able to more accurately diagnose and treat this important clinical problem.

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Appendix: Definition of Epidemiologic Concepts

Sensitivity — the sensitivity of a test is its ability to correctly identify all those with the disease as expressed in the form of a percentage of those with the disease

Specificity — the specificity of a test is its ability to correctly identify all those without the disease as expressed in the forms of a percentage of those without the disease

Positive Predictive Value — the proportion of those with the positive test who have the disease, calculated from a 2 X 2 table of sensitivity and specificity

Post-test Probability — a generic term that defines the probability of disease given a particular result. It may be calculated as a proportion (positive predictive value) or as odds (likelihood ratio).

Likelihood Ratio — for a given level of a test result, the LR expresses the odds that the results come from someone with the disease vs. without the disease. The LR is compared to a nomogram that allows for the determination of post-test probability for any given pre-test probability.

Calculation is as follows:
for test result X:

$$\frac{(\text{No. of patients with disease with X}) / (\text{No. of patients with disease})}{(\text{No. of patients without disease with X}) / (\text{No. of patients without disease})}$$

Raw Data Table (n=286)		
No. of Criteria	Culture Result	
	Positive	Negative
0	3	79
1	8	127
2	7	38
3	6	13

Infective Endocarditis Prophylaxis for Dental Procedures in Patients with Mitral Valve Prolapse

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Abstract

Mitral valve prolapse is a common valvular abnormality and is associated with an increased risk of infective endocarditis. In 1990 the American Heart Association published a series of guidelines and recommendations for the management of infective endocarditis prophylaxis in patients with various cardiac malformations including mitral valve prolapse. We review the evidence supporting these recommendations and the effectiveness of the published guidelines.

Introduction

Mitral valve prolapse (MVP) is associated with an increased risk of infective endocarditis (IE). IE usually has an insidious onset, long course and is often diagnosed quite late - often with disastrous results. Guidelines and recommendations exist for prophylaxis against IE in patients with MVP who are about to undergo dental procedures.

Are these recommendations effective? When is prophylaxis indicated? The objective of this paper is to answer these questions.

Let us begin with a case . . .

Brenda, a married 26 year old mother of a healthy 2 year old boy, is referred to a cardiologist by her family doctor for investigation of a mid-systolic click, suspected to be a prolapsing mitral valve. The patient is to have tooth extraction next week and the family doctor would like to know whether he should recommend antibiotics for infective endocarditis (IE) prophylaxis. Brenda is otherwise healthy, except for persistent lower back pain which

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started after her previous pregnancy. She is currently on no medications except for the birth control pill (Triphasil-28) which she started taking 6 months ago. Brenda has never been hospitalized, except for her previous uncomplicated pregnancy, and has never had surgery. She has no history of serious illness requiring medical attention.

A transthoracic echocardiogram reveals mitral valve prolapse (MVP) with trivial to mild regurgitation at rest. All the chamber sizes were normal and there were no structural abnormalities.

Burden of Illness

MVP is a common valvular abnormality. In fact, it is the most common of the congenital heart lesions affecting approximately 6% of the general population and 12 to 17% of women of childbearing age in industrialized countries.¹ MVP is often an asymptomatic billowing of the mitral leaflets into the left atrium during ventricular systole, the cause being known in only about 5% of cases.² There is an increased familial incidence in some patients suggesting an autosomal form of inheritance, although the exact genetics of MVP are not known.

MVP can occur with and without mitral regurgitation. Depending on the amount of regurgitant flow across the mitral valve during systole, MVP with regurgitation can cause, over time, left atrial enlargement. Asymptomatic in the early stages, atrial enlargement can also persist for years without detection. Ultimately, the patient can suffer from complications due to atrial enlargement, most commonly being arrhythmias of atrial origin.

MVP is also associated with an increased risk of IE. IE is at least fourfold more common in adults with than without MVP. The risk for IE is thought to be further increased by the presence of a mitral regurgitant murmur, male gender, advancing age and probably more severe valvular deformity.³

Etiology

A. Mitral Valve Prolapse

Primary MVP is associated with excessive or redundant mitral leaflet tissue, which usually involves at least half of the anterior leaflet and/or at least two-thirds of the posterior leaflet.³ The excess tissue is a result of myxomatous proliferation of the acid mucopolysaccharide-containing spongiosa layer of the mitral valve leaflet (Figure 1). This proliferation causes focal interruption in the ventricularis layer of the leaflet, which is the basic support for the leaflet. This in turn causes a structural weakness as well as a thickening of the mitral valve leaflet, which facilitates the billowing of the leaflets into the left atrium during systole.³

Secondary MVP occurs without myxomatous proliferation of the spongiosa layer of the valve leaflets. It may be due to relative displacement of ischemic papillary muscles due to transient coronary artery occlusion,³ or it can result from inflammatory changes brought on by rheumatic fever, for example. Our discussion will focus on primary MVP, which is the likely diagnosis in our patient presented in the clinical scenario.

Primary MVP may occur in families where it is inherited as an autosomal dominant trait with varying penetrance.³ The exact genetic etiology of MVP still remains largely unknown.

MVP also occurs in isolated cases, and it has been postulated that primary MVP may be a result of defective embryogenesis of cell lines of mesenchymal origin. This is supported by the observation that there is an association between primary MVP and an increased incidence of coagulopathies (e.g. von Willebrand disease) and various connective tissue disorders. Primary MVP is almost always present in patients with Marfan's syndrome and occurs with higher frequency in other connective tissue disorders, such as Ehlers-Danlos syndrome, pseudoxanthoma elasticum and osteogenesis imperfecta.³

B. Infective Endocarditis due to MVP

The pathogenesis of IE requires several conditions to be present:

- endocardial surface injury;
- thrombus formation at the site of injury (deposition of platelets and fibrin);
- bacterial entry into the circulation;
- bacterial adherence to the injured endocardial surface.

The first two conditions provide an environment which is favorable to infection, while the second pair of conditions permit the implantation of the organism onto the endocardial surface. Therefore, endocardial surface damage is a necessary event for development of IE.² The most common cause of endocardial injury is blood turbulence resulting from haemodynamic abnormalities such as underlying valvular stenosis or regurgitation.³

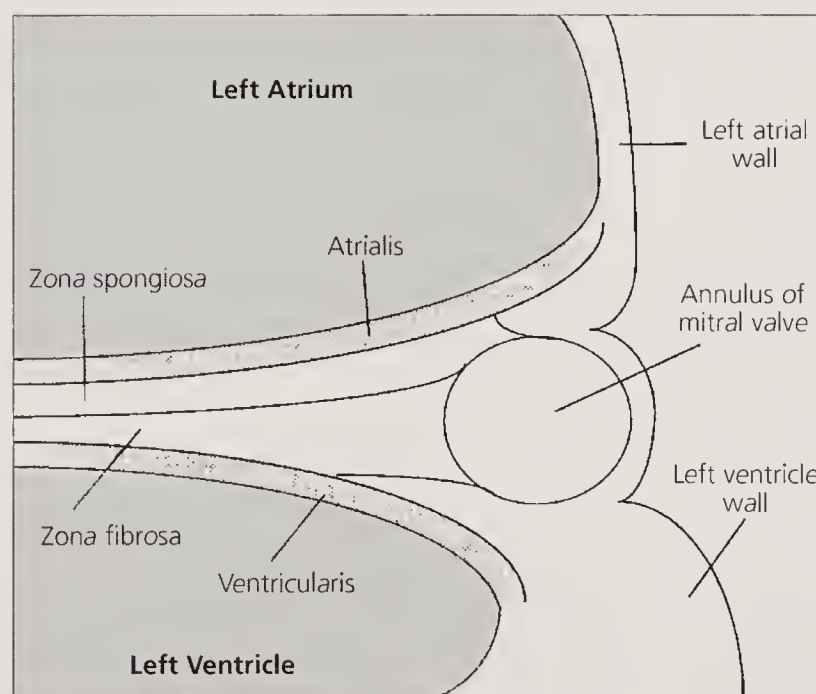


FIGURE 1. Structure of mitral valve leaflet. This is a very strong structure by design as it must withstand left ventricular pressures. It has a strong core of collagen, the zona fibrosa, which is continuous with the annulus of the mitral valve proximally and the chordae tendinae distally. The atrial and ventricular surfaces are covered by continuations of the respective endocardium and are called the atrialis and ventricularis, respectively, the latter being rich in elastic tissue. Between the atrialis and the zona fibrosa is the zona spongiosa, which contains collagen, cardiac muscle cells, capillaries, neural elements, connective tissue and is rich in proteoglycans.

Most cases of IE are caused by α -haemolytic streptococci, such as *Streptococcus viridans*, which are common oral bacteria. *Staphylococcus aureus* and *Staphylococcus epidermidis*, as well as gram negative bacilli are becoming more common causes.⁴ *Enterococcus faecalis* and *Enterococcus faecium* are also seen in cases of acute and subacute IE.⁴

The incidence of IE is 11 to 50 cases per million population per year.² Before the introduction of antibiotics, the mortality rate for IE was almost 100%. Now the mortality rate for endocarditis caused by α -haemolytic (viridans) streptococci is below 10%, and rates for IE resulting from the other less common organisms are 40% to 80%.² Surprisingly, there has not been a decline in the incidence of IE since the pre-antibiotic era.⁵

Table 1
The 1990 American Heart Association
Recommendations for Dental Procedure Prophylaxis

Standard Regimen

Amoxicillin, 3 g orally, 1 hour before procedure; then 1.5 g 6 hours after initial dose.

Alternative Regimen for patients allergic to amoxicillin and penicillin
Erythromycin ethylsuccinate, 800 mg, or erythromycin stearate, 1 g, orally
2 hours before procedure; then, half a dose 6 hours after initial dose;

or

Clindamycin HCl, 300 mg orally, 1 hour before procedure, and 150 mg
6 hours after initial dose.

Initial Pediatric Doses

Amoxicillin, 50 mg/kg; erythromycin ethylsuccinate or erythromycin
stearate, 20 mg/kg; clindamycin, 10 mg/kg. Follow-up dose is one half
of initial dose. Total dose should not exceed total adult dose.

Adapted from Dajani et al. (1990).⁸

IE appears to be associated only with extractions, sealing or surgery involving gingival tissues.⁶ The Working Party of the British Society for Antimicrobial Chemotherapy⁷ and the American Heart Association (AHA)⁸ therefore recommend that prophylactic antibiotics be given for these procedures only.

In 1990, the AHA published a series of guidelines and recommendations for the management of IE prophylaxis in patients with various cardiac malformations, including MVP. However, the AHA guidelines (Table 1) are not based on any controlled clinical studies in humans but rather on clinical experience, *in vitro* studies and animal studies. Therefore, do we know if dental procedures actually cause IE in the presence of MVP in humans? Bayliss *et al.* (1983) reviewed 200 cases of viridans streptococcal endocarditis and reported 13% of patients had dental procedures within 3 months of diagnosis and 8% had dental treatment within 1 month.⁹ A review of 1,300 cases of IE reported that only 4% had dental extractions within the previous two months.¹⁰

Therefore, it can be argued that there is a temporal association between exposure (i.e. dental procedure) and the diagnosis of IE, suggesting a causal effect. However, the vast majority of cases of IE are not caused by dental procedures. It has been reported that bacteremia occurs in 40% of patients after dental extraction but also develops in 25% after toothbrushing or oral irrigation, and in 38% with normal chewing. Furthermore, it has been calculated that the cumulative relative risk for bacteremia was 1,000 fold greater after self-manipulation than after dental extraction.¹⁰

Given these relative rates of bacteremia, it is obvious that some of the burden associated with IE due to MVP can be avoided by good oral health care. The AHA recommends good oral hygiene consisting of brushing, flossing, and use of fluoride rinses and antiseptic mouth washes before dental procedures. Regular and careful dental care is clearly important for those with known MVP with regurgitation.⁹ The AHA also recommends that topical antiseptic treatment be given after prophylactic antibiotics, because irrigation itself may cause bacteremia.⁸ Access to good oral health therefore, is an important issue when dealing with IE in MVP and yet is inaccessible to many in our society.

Another interesting aspect of IE prophylaxis is the fact that there are certain risks associated with the recommended antibiotic use. These include gastrointestinal upset, infection by resistant organisms, cross-reactivity with other drugs, and allergic reactions, including anaphylaxis and death.

It has been previously reported that three prophylactic erythromycin regimens for IE given 1 week apart led to development of resistant oral streptococci in all subjects and persisted for 23 to 42 weeks.¹¹ A single dose of amoxicillin given every week for 4 weeks caused a significant increase in streptococcal resistance, so single antibiotic treatment would not be effective if endocarditis did occur.¹² Based on Harrison's work, the AHA made the following recommendations, if a series of dental treatments is necessary: the dentist is to 1) leave an interval of at least 7 days between procedures to restrict the emergence of resistant organisms; and 2) complete as much work as possible during each dental visit.^{11,12}

Lastly, Pallaseh concluded that if dental treatment is assumed to be routinely responsible for IE and if all patients with MVP who are undergoing dental procedures received prophylactic penicillin, the risk of death would be greater from penicillin anaphylaxis than from IE.^{13,14} This conclusion caused the AHA to recommend prophylaxis for MVP only if a systolic murmur (i.e. regurgitation) exists.

Community Intervention Effectiveness

MVP with regurgitation can be diagnosed by auscultation of a midsystolic snap and a late systolic murmur. However, MVP is typically diagnosed (or the diagnosis is confirmed) using transthoracic echocardiography. Diagnostic criteria using motion and morphology can separate patients with and without prolapse with a high degree of sensitivity (>95%) and specificity (>95%) and identify those at risk for complications.¹⁵

Patients with primary and secondary MVP must be distinguished from those with normal anatomic variations on echocardiography. These variations can result in an incorrect diagnosis of MVP, particularly in patients who are hyperkinetic or dehydrated on auscultation during the physical examination, or during the two-dimensional echocardiography.¹⁵ Other auscultatory findings may be misinterpreted as midsystolic clicks or late systolic murmurs. Patients with mild to moderate billowing of one or more nonthickened leaflets toward the left atrium with the leaflet coaptation point on the ventricular side of the mitral annulus, and no or minimal regurgitation by Doppler echocardiography are probably normal.¹⁵ Unfortunately, many such patients with neither a nonejection click nor murmur of mitral regurgitation are frequently misdiagnosed as having MVP.¹⁵

The issue of dentist, patient and physician education about the AHA guidelines should also be considered. In a recent survey, it was found that 15% of dentists surveyed never asked their patients about a history of heart murmur, and when presented with this history, only 50% routinely consulted with the patient's physician.¹ A 1989 survey showed that only 39% of responding dentists and only 27% of responding physicians adhered to the guidelines that existed at that time.⁵

Many of the physicians who did not adhere to the AHA guidelines based their practice on the observation that half of the patients who contracted IE had no previous "at risk" condition, which would have indicated prophylaxis. Furthermore, only a fraction of endocarditis cases are caused by organisms of oral origin. Theoretically, only 10% of cases of oral IE are preventable.^{9,16} Physicians and dentists are asking themselves "Are we giving antibiotic cover purely for defensive medico-legal reasons?" It is commonly felt that if we continue to overuse antibiotics the problems of resistant organisms, drug interactions and hypersensitivity can only increase.¹⁶ Although these concerns can be only partially answered, the overall clinical benefit of IE prophylaxis has not been thoroughly investigated.

Cost-Effectiveness of IE Prophylaxis for Patients with MVP

Earlier studies show that the clinical benefit or cost-effectiveness of IE prophylaxis for MVP patients was slight or even deleterious in studies performed in the early 1980's. However, when one looks at the recent literature after the AHA published its recommendations in 1990, one finds only two studies that re-address this issue, and they are both in complete contrast to the previously published works.

Devereux *et al.* (1994) showed that the calculated costs associated with peridental antibiotic prophylaxis of MVP patients with a mitral systolic murmur (\$3,000) were lower than the estimated costs per year of life saved of \$29,000 to \$66,000 for treatment of hypertension, \$95,000 for coronary bypass surgery for 3-vessel disease and \$47,000 to \$117,000 for cholesterol-lowering drug therapies.¹⁷ Thus, peridental antibiotic prophylaxis for MVP patients with a mitral regur-

gitant murmur is reasonable from the standpoint of health-care policy as well as individual benefit.¹⁷

Calculations for MVP without mitral systolic murmurs suggests that the ability to prevent IE with antibiotics is low (a net of 9.8 cases prevented with amoxicillin per million dental procedures) and costly.¹⁷ Therefore IE prophylaxis in this patient group is not warranted.

Gould and Buckingham (1993), have also found the practice of antibiotic prophylaxis to be highly cost-effective.¹⁸ They reported that for every 10,000 extractions in "at risk" patients appropriate prophylaxis prevented 5.7 deaths and a further 22.85 cases of non-fatal IE. This represented a savings in hospital care costs of £289,600 for 10,000 extractions.¹⁸

The issue of cost-effectiveness of IE prophylaxis needs to be re-addressed and measured within the context of a Canadian health care system. How applicable are the American and British studies to a Canadian patient? Despite the controversy surrounding some of the issues outlined above, the practise of IE prophylaxis with antibiotics given to patients with MVP prior to a dental procedure, does more good than harm to a patient. The actual economic benefit derived in Canada has yet to be measured.

Synthesis and Implementation

Given the AHA and British recommendations, and knowing the controversies discussed in this report, what should we do for our patients?

The primary care giver, in documenting the presence of MVP in a patient, must determine if it is present with or without regurgitation. This may require echocardiography if auscultation is difficult. Although echocardiography adds to the health care costs of the patient, it is necessary to make this distinction since it will determine whether or not the patient will require IE prophylaxis.

Regardless of the patient's final diagnosis, good oral hygiene must be emphasized. In addition, communication with the patient's dentist will ensure that the proper technique will be demonstrated, and the necessary patient education will be reinforced. Furthermore, including the dentist as part of the health care team will facilitate exchange of timely information ensuring patient welfare.

The data available on the efficacy of the AHA guidelines, thus far, support their use. The protective efficacy of the recommendations from the AHA if followed, is estimated to be 91%.¹⁹ Therefore, strict adherence to the guidelines should be encouraged among physicians and dentists. Patients should be told of the need for prophylaxis and, if necessary, an "Endocarditis Risk Card" can be devised and supplied to the patient, thereby facilitating communication with other allied health care professionals.

As with other aspects of preventative medicine, education regarding general health must be encouraged. Specifically in

patients with MVP, issues surrounding intravenous drug use, smoking and alcohol use should be addressed.

Monitoring

A recent survey of 189 “at risk” patients revealed 50% had told a dentist about their heart condition.²⁰ This underscores the need to educate patients about their own health. Only 8% were aware of a dental problem and 39% had not attended a dentist in 5 years.²⁰ The accessibility to dental care is a real issue, since many patients without dental plans or sufficient disposable income cannot benefit from routine dental cleanings.

Of the 262 physicians surveyed, 50% took a dental history but only 3% gave antibiotic advice in writing.²⁰ Only 57% of surveyed physicians prescribed antibiotics recommended by the British Society for Antimicrobial Chemotherapy⁷ and 50% of physicians and dentists surveyed were unaware of some of the cardiac conditions requiring prophylaxis.²⁰

In order for the AHA recommendations to work, it is imperative that physicians and dentists work together to ensure that patients are getting the information they need. Health care workers must also ensure that they themselves are providing the appropriate care to patients at risk.

What about Brenda?

Given the echocardiographic findings, it is recommended that Brenda be given the benefits of IE prophylaxis with the administration of peridental antibiotics. In order to ensure patient compliance, the physician should contact the dentist expressing concerns about the patient’s risk for IE and ask for the dentist’s opinion and recommendations.

Patient education is an important part in reducing IE risk related to MVP. Therefore, the need for excellent oral hygiene should be emphasized to Brenda. Instruction should be given to her by either the dentist or the dental hygienist on proper cleaning and flossing. Given that Brenda has already presented with the need for a tooth extraction, she is most likely in need of re-education on proper oral hygiene.

Concluding Remarks

Further study into the efficacy and cost-effectiveness of IE prophylaxis for dental procedures in patients with MVP is needed. There are no randomized controlled clinical trials and no Canadian studies that address this issue. Instead, much of the policy surrounding IE prophylaxis is based on clinical experiences and medico-legal issues instead of scientific data. Nonetheless, the data that is available tends to support the use of the published AHA guidelines for antibiotics for IE prophylaxis. The use of these antibiotics is thus far supported by the literature, even when analyzed for either risk to the society with resistant strains of organisms, or to the community with health care costs, or to the patient with adverse and allergic reactions to the antibiotics.

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In the Literature

No Link Between Power Lines and Leukemia

Since 1979, when studies found an increased incidence of leukemia in children living near power lines, there has been controversy over the link between electromagnetic fields and cancer. A recent case-control study (*N Engl J Med* 1997;337:1-7) may finally settle the issue. In this study, 638 children with acute lymphoblastic leukemia (ALL) and 620 controls were followed for exposure to magnetic fields. In the subjects' current and former homes, researchers blinded to the subjects' health status measured magnetic field levels over a 24 hour period. The distance and configuration of nearby power lines was also investigated. The risk of childhood ALL was found not to be linked to magnetic field levels or the distance and configuration of power lines, either in subjects' current homes, or in the homes where their mothers had lived while pregnant.

NO Therapy for Sickle Cell Disease?

A new study (*J Clin Invest* 1997;100:1193-1198) by researchers in Boston suggests that inhaled nitric oxide (NO) gas may successfully treat sickle cell disease (SCD), a genetic condition characterized by severe hemolytic anemia, vasoocclusive episodes and shortened life span. Low concentrations of NO were found to increase the oxygen affinity of sickle erythrocytes both *in vitro* and *in vivo*, without significant production of toxic methoxyhemoglobin. In addition, no effect was seen on the oxygen affinity of normal red cells exposed to NO. Increasing the oxygen affinity of hemoglobin S (HbS) decreases the formation of HbS polymers within red cells, thereby reducing sickling and disease. The next step will be to conduct a randomized double-blind study to examine the long-term effects of NO on SCD patients.

Novel Strategy Blocks HIV Infection

Over the past two years, chemokines (chemotactic cytokines) and their receptors have been the focus of intense research

regarding their apparent anti-HIV properties. Two recent reports (*Nature Med* 1997;3:1110-1116 and *Proc Natl Acad Sci USA*, in press) describe the use of genetically modified chemokines ("intrakines"), which remain in the cell's endoplasmic reticulum, to prevent chemokine receptors from reaching the plasma membrane. Chemokine receptors such as CXCR4 and CCR5 have previously been shown to function as essential co-receptors for HIV infection of T lymphocytes. By sequestering receptors, the researchers were able to confer *in vitro* HIV resistance to T cells expressing the intrakine. Although clinical trials are years away, the combination of intrakine gene therapy and drug cocktails may hold the key to the effective treatment of HIV infection and AIDS.

p53 Tumour Suppressor Has a Sibling

P53, the famous tumour suppressor gene mutated in 60% of human cancers, is single no more. A new study (*Cell* 1997;90:809-819) has identified p73, a novel gene located on a region of chromosome 1 (1p36) frequently deleted in neuroblastoma and other cancers. P73 contains many of the same protein domains as p53, and is thought to function as a transcription factor. However, while p73 appears to play a role in growth suppression, it lacks p53's ability to respond to DNA damage and exhibits monoallelic expression. Research will now focus on the elucidation of p73's role in normal and malignant cell growth and development.

Does KSHV Cause Multiple Myeloma?

Multiple myeloma, the second most common blood malignancy in the US, is caused by Kaposi's Sarcoma-Associated Herpesvirus (KSHV), according to a recent report (*Science* 1997;276:1851-1854). KSHV was found in dendritic cells of myeloma patients, but not in malignant plasma cells or dendritic cells from normals or patients with other cancers. Viral

interleukin-6 (vIL-6) was found to be produced by infected patients' dendritic cells. IL-6 is already known to be a growth factor for myeloma. These findings imply that KSHV may cause myeloma by "remote control," driving the growth of malignant plasma cells via vIL-6 secretion. The authors suggest that KSHV may play a causative role in the transformation of a precursor condition, monoclonal gammopathy of undetermined significance (MGUS), to multiple myeloma. Whether KSHV is the sole etiologic agent in multiple myeloma remains to be proven.

Medical Students in the Community

A study conducted at University College London Medical School in England, and published in the October 10, 1997 *British Medical Journal* concluded that medical students "can learn clinical skills as well in general practice as in the hospital." The study was conducted in response to what the authors view as an international move towards community based undergraduate medical education. Medical students were divided into two groups, one received clinical training in the community and the other received clinical training in a hospital setting. The success of the learning experiences were measured using objective structured clinical examinations (OSCE). Differences in OSCE scores between the two groups were found to be statistically not significant. According to the authors of the study, these data support efforts to redistribute resources from traditional locations for student learning to the community.

Source: Murray E. et al. (1997) *BMJ* 315: 920

Parkinson's Disease Gene Identified

In 1817, the British physician James Parkinson first described the eponymous disease which is characterized by slowness and poverty of movement, muscular rigidity, resting tremor and postural instability. Until recently, it was believed that environmental factors were largely responsible for the disease which results in death of dopaminergic neurons. However, last November, researchers from the National Institutes of Health, Robert Wood Johnson Medical School, Italy, and Greece reported that Parkinson's Disease in an Italian family showed strong linkage to a region on chromosome four. That discovery was followed-up by a June publication in *Science* which identified a mutation in the gene coding for α -synuclein in one Italian and three Greek kindreds with the disease. Although the function of α -synuclein is not known it is thought to be important in neuronal plasticity.

Source: Polymeropoulos M. et al. (1997) *Science* 276: 2045

Lack of Job Control Deadly

It has been appreciated for quite some time that there is an inverse relationship between social class and most health outcomes. The landmark Whitehall study showed an inverse social gradient in mortality from coronary artery disease among British civil servants. However, known coronary risk factors account for only about 25% of the observed variation. A study published in *The Lancet* in July assessed the contribution of psychosocial work environment to the social gradient. The study found that the largest contribution was from low control at work. The investigators concluded that greater attention to the design of work environments may be an important way to reduce inequalities in health.

Source: Marmot M. et al. (1997) *Lancet* 350: 235

Obesity Medication Linked to Heart Disease

A commonly prescribed combination of drugs used in the treatment of obesity has been found to cause valvular heart disease. The combination of fenfluramine and phentermine (colloquially known as "phen/fen") had been implicated in 33 cases of mitral, aortic and tricuspid valve disease according to a July 8, 1997 letter. In 1996, a total of 18 million monthly prescriptions were written for fenfluramine or phentermine. Both drugs have been approved by the FDA to treat obesity alone, but the widely used combination has not been approved and it thus an "off label" use. The FDA asked that fenfluramine and a similar compound, dexfenfluramine be withdrawn.

PARP Implicated in Stroke Pathogenesis

It has long been known that after stroke, nitric oxide (NO) plays an important role in secondary neuronal injury and death. However, investigators at Johns Hopkins have recently shed light on the precise mechanism whereby NO exerts its deleterious effects. Their investigations point to poly(ADP-ribose) polymerase (PARP). PARP catalyzes the attachment of ADP-ribose units to nuclear proteins after DNA damage. After small amounts of DNA damage, PARP is recruited to help repair the damage. However, with the more substantial damage which occurs after stroke, PARP can be overactivated. Excessive activation of PARP leads to depletion of cellular ATP and NAD reserves. In the study, knockout mice lacking the gene coding for PARP were found to be as resistant against glutamate-mediated neurotoxicity as they were to injury due to reversible middle cerebral artery occlusion. These studies suggest that "therapies designed towards inhibiting PARP may provide benefit in the treatment of cerebrovascular disease."

Source: Eliasson M. et al. (1997) *Nature Med* 3: 1096

The Changing Face of Leprosy: Insights from India

Abha Gupta, MSc. (OT0) and Jay S. Keystone, MD, MSc. (CTM), FRCPC

Historically, leprosy has imprinted itself on humanity as an insidious, slowly-developing condition resulting in terrifying physical mutilation and social ostracism. Medically, leprosy is a chronic infection caused by *Mycobacterium leprae* which attacks superficial tissues, particularly the skin and peripheral nerves. The suspected mode of transmission is thought to be via inhalation of bacilli-laden dust particles that enter the upper respiratory tract. Leprosy is not easily communicable, and more than 90% of the world's population are naturally immune. Thus, few in contact with infectious individuals actually develop the disease. Environmental factors such as poor hygiene and crowded living conditions, however, may contribute to the spread of leprosy.

The clinical course of the disease encompasses a wide spectrum of signs and symptoms depending on the extent of the host's cellular immune response to the infection. Most individuals, however, are unable to develop a sufficient cell-mediated immune response, and the bacilli disseminate throughout the body causing the more severe, highly infectious lepromatous leprosy. This lack of immunity is specific to *M. leprae* and is not associated with a generalized decrease in cell-mediated immunity. In those patients left untreated, there can be widespread damage to the extremities mostly because of marked anesthesia and deformity, especially in the ulnar, medial and common peroneal nerve regions, subsequent repeated trauma, and secondary infection.

At one time every continent was plagued with leprosy, but now it is restricted to the poverty belt of the globe, predominantly in India, Indonesia, Myanmar and Africa. In 1981, in order to combat increasing dapsone resistance, the World Health Organization (WHO) recommended Multi-Drug Therapy (MDT), a cocktail consisting of rifampin, clofazimine and dapsone which cures all

forms of leprosy. With the advent of MDT, the estimated number of registered leprosy cases worldwide has fallen from 5.5 million in 1991 to less than 1 million in 1996. More than 50% of these cases are found in India.¹

In 1994, the WHO initiated an organized effort to attain the "global elimination of leprosy as a public health problem by the year 2000."¹ The National Leprosy Elimination Program (NLEP) is an initiative engineered by the WHO which strives to reach this goal by executing intensive case detection and improving the implementation of MDT. This program has been organized in countries which have a high incidence of leprosy, including India.

In the North Central Indian city of Bhopal, which is infamous for its 1985 Union Carbide chemical disaster, the NLEP has been in full swing since 1994. Individuals are diagnosed with leprosy through door-to-door population surveys conducted by trained NLEP personnel or through physician consultation, and are referred to one of many NLEP centres located throughout the city. Here the patients arrive on a specified day each month and receive a free 28-day supply of MDT. This regimen effectively cures patients with leprosy after a drug course lasting 6 or 24 months, depending on the patient's type of leprosy.

In the past, individuals who were diagnosed with leprosy were stigmatized and socially isolated and were sent away from their communities to live in leper-colonies. Today, for the 454 patients registered with the NLEP in Bhopal district, a diagnosis of leprosy is not detrimental to the lifestyle of the individual. Leprosy patients continue to live with their families and conduct their daily activities as they did before they were diagnosed with the disease. Early diagnosis, the availability of an effective cure, economic necessity and the lack of disease-awareness all play a role

in preserving the quality of life of those treated for leprosy. The intensive case detection strategies and population surveys of the NLEP have led to the very early diagnosis of leprosy. In the majority of cases, the disease has been identified before irreversible deformities set in, with patients presenting only with patches of anesthesia and/or hypopigmentation in the upper and lower limbs. Therapeutic intervention prior to physical impairment is important in maintaining the employment abilities of individuals, and thus avoids additional economic distress. Also, the mild clinical presentation reduces the fear that friends and family members of patients have of acquiring the disease and prevents social isolation of the affected individual.

The development of a cure for leprosy has contributed to the decreasing incidence of infection. After the initial few doses of rifampin, regardless of the stage of disease, patients lose their ability to infect others and prevent further community spread. Thus, for leprosy patients undergoing treatment, there is no need for a change in lifestyle and patients can remain part of the social network within their community.

Generally, patients in Bhopal are poorly educated and of very low socioeconomic status. They belong to large families and are commonly employed as street sweepers, general laborers, and farmers. A small proportion of these individuals do have visible deformities including ulnar contractures, active ulcers on the hands and feet, and missing digits. However, socioeconomic burdens outweigh any fears associated with contracting the disease. Family members cannot afford to alienate an affected person, especially men, since infected men are still considered vital resources. An affected family's financial stress reinforces their need for each other to the extent that the impact of disease becomes inconsequential. It is interesting to speculate whether leprosy patients and their families in the educated, upper class receiving private treatment are as comfortable with their condition.

Interestingly, the most significant factor in maintaining the quality of life of infected individuals after they have been diagnosed with leprosy in Bhopal is their lack of disease awareness. The majority of patients in the Bhopal district registered with NLEP have absolutely no knowledge of their condition. Actively contributing to this lack of disease awareness is the reluctance of NLEP workers to fully disclose the diagnosis of leprosy to affected individuals. Patients are told that they have a "skin disease" that will be cured if the medication being given is taken properly. The mandate of NLEP is to improve case detection and implementation of drug therapy, and full disclosure would impede this process. Telling patients that their benign symptoms are a result of leprosy would only serve to instill denial, anger towards NLEP personnel and possible social isolation. This reaction would interfere with patient accessibility, quality of life, and drug compliance, thus compromising the program's efficacy at eliminating the disease.

The fear and aversion that historically has been associated with leprosy still looms in the minds of many people. These

feelings bring psychosocial distress to patients and their families. However, as patients and their families do not know that leprosy is even a possible diagnosis, most patients are not hesitant to inform family members, friends and co-workers that they are taking daily medication for their dermatological symptoms. The lack of disease consciousness has greatly reduced the physical and psychological burden associated with leprosy.

The non-disclosure of the diagnosis of leprosy is an interesting and controversial approach to destigmatizing leprosy. Perhaps it also works well since patients tend to delegate the responsibility of their health directly to the doctor, feeling no curiosity for details. North American medical practice, on the other hand, demands full disclosure, and such strategies would not be feasible in our society from an ethical and medical-legal perspective.

The dedication of NLEP team members in Bhopal, a city of 1.62 million, has effectively decreased the number of registered leprosy cases from 1,696 in 1993 to 454 in 1997, a prevalence of 3.36 per 10,000.² The goal of the NLEP as part of the WHO elimination program is to reach a prevalence of 1 per 10,000 by the year 2000. Patients are diagnosed and receive treatment within their communities and at no time are they asked to deviate from their daily living habits. Early diagnosis, effective treatment, economic necessity, and above all, the lack of disease awareness amongst leprosy patients preserves the quality of life experienced by patients being treated for leprosy in Bhopal. If case detection and subsequent treatment compliance remain high, and if the determination of the individual workers in NLEP persists, India and other affected countries may soon realize their goal of eliminating leprosy as a public health disease.

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The Role of HIV Chemoprophylaxis Following Occupational Needle Stick Injury

Moss Weinstock (9T8), Jeff Weissberger (9T8) and Mark Weinstock BSc.

Introduction

It is estimated that the 4.4 million health care workers in the United States receive 800,000 needle stick injuries annually. Approximately 16,000 of these sharp objects are contaminated with human immunodeficiency virus (HIV).¹ As future health-care professionals working in Emergency Rooms, Occupational Health Departments and the community, we will be called upon to provide advice regarding post-exposure prophylaxis. The counselling, educational and psychological support available for those at risk of HIV infection will benefit from health care workers' (HCW) familiarity with the current research in this area. This article focuses on current strategies and effectiveness of HIV chemoprophylaxis following needle stick injury.

Current data indicate that medical students receive percutaneous injuries at least as often as other health care providers.¹ Forty-eight percent of all graduating medical students reported being exposed to potentially contaminated body fluids during the last two years of medical school.² In addition, 27% of medical students incurred injury by sharp objects or had mucocutaneous exposure of body fluid during the previous six months of clinical rotations.³

The sequelae can be catastrophic for infected students. The potential risks include the inability to practise in the profession of their choice, the inability to obtain life or disability insurance, long term illness and premature death. Furthermore, infected medical students fail to qualify for Workers' Compensation and are left to face devastating illness and high pharmaceutical expenses without financial assistance.

Resources

A MEDLINE search (of English language articles) retrieved information from the years 1983 to 1997 under the MeSH headings of HIV, AIDS and medical students with subheadings *prevention and control*, and *etiology and epidemiology*. The Yahoo! search engine was used to explore Internet resources and the recommendations of the Center for Disease Control (CDC) were reviewed. Experts in the

Department of Occupational Health at Sunnybrook Health Science Centre in Toronto, Ontario, were consulted as were workers at the AIDS Counsel of Toronto (ACT). Additional data were obtained from the Canadian Foundation for AIDS Research (CANFAR) and the Laboratory Centre for Disease Control, Health Canada. Due to the great global interest in the topic, extensive literature was available through MEDLINE and the Internet regarding risks of HIV transmission and needle stick injuries. Despite the large quantity of published material, information was limited by the absence of prospective, randomised, controlled studies involving human subjects.

Results

The modes of HIV transmission have been well documented, each with its own rate of transmission.⁴ Needle stick injury accounts for less than 1% of current HIV infections in Canada.⁵ The probability of HIV infection following puncture with an HIV contaminated needle is only 0.0032.⁶ Certain factors increase the risk of transmission (with adjusted odds ratios in parenthesis): deep injury (16.1), visible blood on the device (5.2), the involvement of a source needle placed directly in a vein or artery of the patient (5.1), and the source patient suffering from terminal illness (6.4).⁷

Several studies indicate that post-exposure treatment with zidovudine (AZT) can prevent retroviral infection in mice and cats.⁸⁻¹⁰ However in primates, the evidence has not indicated any treatment effect of prophylaxis with licensed anti-retroviral drugs.¹¹ AZT is an effective prophylactic drug in reducing HIV transmission in the perinatal period,¹² providing a human model of HIV prophylaxis. The best available study regarding chemoprophylaxis following needle stick injuries comes from the CDC Morbidity and Mortality Weekly Report (MMWR).⁷ This study assessed 31 health care workers who became HIV positive following percutaneous exposure to HIV contaminated body fluids. When compared with 679 control HCW who remained seronegative following such exposure, AZT was found to reduce the risk of HIV infection among HCW by

approximately 79% (95% C.I. = 43%-94%). On the basis of these studies and the known efficacy of other anti-virals with HIV infections, the CDC established treatment guidelines¹³ which have been clarified by Gerberding (1996).⁶ Generally, chemoprophylaxis involves the use of AZT 200 mg tid and lamivudine (3TC) 150 mg bid beginning from 2 to 72 hours following exposure and continuing for 28 days. For higher risk exposure, indinavir 800 mg q8h is added.

Critique

The animal studies mentioned above were performed using the retroviruses feline leukemia virus and simian immunodeficiency virus (SIV), not HIV. Therefore, this data may not be directly applicable to humans who have been exposed to HIV. The primate studies revealed no protective effects from AZT prophylaxis. However, these studies did not completely parallel needle stick injuries. The titre of virus used was substantially higher than would be encountered in occupational exposure and the animals were inoculated intravenously. This would bypass potentially important subcutaneous host defences such as Langerhans' cells or dermal dendritic cells.¹⁴

The MMWR human study had many strengths. Being both multi-centred and multi-national, it eliminated potential regional bias. Using statistical manipulation, the study also controlled for different variables such as the extent of exposure to contaminated body fluids and the depth of injury. It included a sufficient number of cases (31 cases with HIV seroconversion and 679 controls without seroconversion) to produce statistically significant results. However, this study had methodological flaws. It was a retrospective case-control study and not a prospective, randomised control trial. There was no placebo control and the patients, physicians and evaluators were not blinded. This made the results vulnerable to reporting bias and ascertainment bias. Furthermore, the cases and controls were not matched and came from entirely different sources. The cases were obtained from mandatory reporting requirements while the controls were obtained through a passive surveillance system that could have produced a selection bias.

The recommendations for prophylaxis are not based on type 1 evidence, evidence obtained from at least one properly designed randomized controlled trial.¹⁵ In fact, because the incidence of seroconversion after needle stick injury is 0.003, a sufficiently powerful prospective randomised controlled trial would not be feasible.¹⁶ The information supporting the use of AZT is based on type 2 evidence obtained from a well-designed cohort analytic study. Beneficial effects from the inclusion of other anti-virals in the prophylaxis after needle stick exposure are based on theoretical considerations and opinions of the authorities in the field, type 3 evidence.

Another strength of the MMWR study was its consideration of the side effects of AZT. Nausea, fatigue, headache and gastrointestinal distress were frequently experienced and their effect on otherwise healthy employees was a cause for concern. Approximately one third of patients discontinued the AZT treatment because they could not tolerate the side effects.⁶ Additionally, the numbers treated with AZT were too few to detect any rare but serious side effects.

Finally, the cost-effectiveness of prophylaxis has not yet been established.⁶ The cost in the USA of 30 days of treatment is

\$278.64 with AZT, \$223.92 for 3TC and \$360.00 for indinavir.¹⁷ The lifetime medical costs of treating HIV and AIDS has been estimated at \$119,000.¹⁸

Conclusion

Needle stick injuries are a common and consequential risk in the health care community. Approximately 4.4 million health care workers in the USA receive 800,000 needle stick injuries each year. Of these, approximately 16,000 are contaminated with HIV. Furthermore, forty-eight percent of all medical students recall being exposed to potentially contaminated body fluids during their final two years of training. The risk of transmission of HIV via contaminated needle sticks is small but genuine (0.003). This danger is increased when large amounts of blood are involved, when the injury is deep, and when the patient suffers from advanced AIDS. The risk of HIV transmission was reduced by 79% using AZT as post-exposure chemoprophylaxis. The combination of AZT, 3TC and indinavir has been recommended as prophylaxis by experts in the field. It is advised that chemoprophylaxis be instituted on an urgent basis between 2 and 72 hours post-exposure, and that treatment be continued for 28 days. However, no study has demonstrated increased efficacy with combination therapy over AZT alone. As well, there have been no randomised control studies examining chemoprophylaxis.

Needle stick injuries are common among health care workers, with the potential of leading to tremendous physiological and psychological consequences. Chemoprophylaxis can provide a valuable element in the treatment of an injured health care worker by significantly reducing the risk of HIV infection and AIDS.

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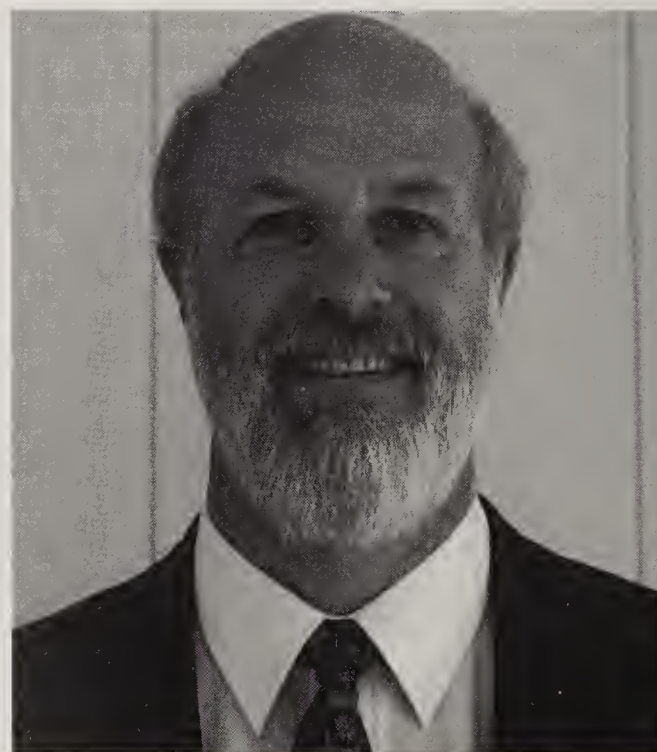
The Gairdner Awards

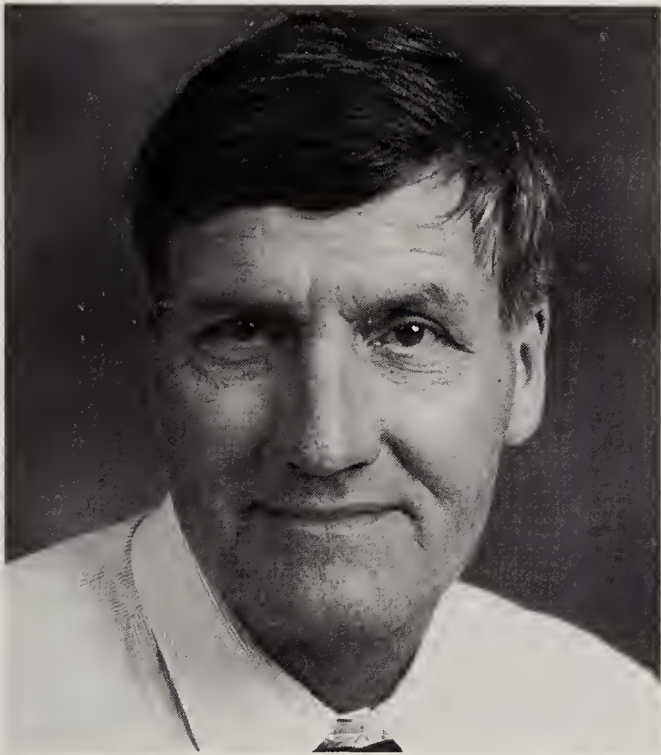
In 1957, the late James A. Gairdner (1893-1971) established the Gairdner award to recognize outstanding contributions to medical science by scientists whose work has contributed significantly to improving the quality of human life. This year's winners are Dr. Corey Goodman, Dr. Richard Hynes, Dr. Erkki Ruoslahti and Dr. Alfred Knudson, Jr. To date, the Gairdner Foundation has made 247 awards. Forty-nine of the awardees have later received the Nobel Prize, 27 of these in the last fifteen years.

Dr. Richard Hynes is being recognized jointly with Dr. Erkki Ruoslahti for their discovery and characterization of the molecular basis of interaction between cells and the extracellular matrix. Dr. Ruoslahti has focused on peptide mimics of adhesion proteins and, more recently, signal transduction aspects of interactions between cells and their extracellular matrix. Dr. Hynes has used genetic approaches to analyze the functions of fibronectin and integrins, and has identified critical roles for these proteins in embryogenesis. Their work holds promise for development of novel therapies for a number of diseases including thrombosis, inflammation and cancer.

Richard O. Hynes, Ph.D

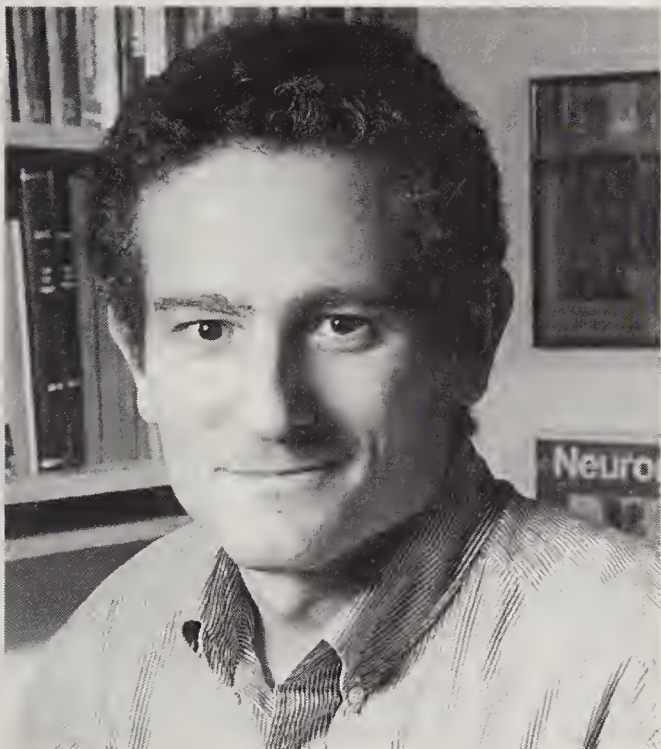
Dr. Hynes was born in Nairobi, Kenya and educated at the University of Cambridge, England. He received his BA in 1966 and his MA in 1970, both in biochemistry. Subsequently, he received his Ph.D from M.I.T. in 1971. He is now an investigator of the Howard Hughes Medical Institute and Head of the Biology Department and Director of the Center for Cancer Research. Dr. Hynes is a Fellow of the American Association for the Advancement of Science, the Royal Society of London as well as the American Academy of Arts and Sciences.





Erkki Ruoslahti, MD, Ph.D

Dr. Ruoslahti was born in Puumala, Finland. He received his MD in 1965 and a Ph.D in Immunology in 1967. Dr. Ruoslahti has lived in the United States since 1976. He is now the President and Chief Executive Officer of The Burnham Institute in La Jolla, California as well as Adjunct Professor in the Department of Pathology at the University of California, San Diego. Dr. Ruoslahti is a Fellow of the American Academy of Arts and Sciences and has been the recipient of the Outstanding Investigator Award of the National Cancer Institute.



Corey S. Goodman, Ph.D

Dr. Goodman, Professor and Head of the Division of Neurobiology at the University of California at Berkeley, is a developmental neurobiologist who has made substantial contributions to the field of neurodevelopment through his novel and creative studies on the molecular basis of axon guidance. His research has focused on the molecular mechanisms that control brain wiring, with special interest on how neurons find their targets and make the correct synaptic connections in the developing nervous system. His pioneering studies in *Drosophila* identified many of the genes involved in axon pathfinding and synaptic plasticity. His group subsequently identified the human homologues of these brain wiring genes, which may provide clinical insights into neurological disease and spinal cord regeneration.



Alfred Knudson, MD, Ph.D

Dr. Knudson is a Distinguished Scientist at the Fox Chase Cancer Center in Philadelphia and Adjunct Professor of Pediatrics and Human Genetics at the University of Pennsylvania School of Medicine. His work on the development of a two-hit mutational hypothesis for retinoblastoma and other cancers has greatly advanced our understanding of tumorigenesis. His hypotheses, which combine both mathematical and medical insights, have become paradigms for mutational theories on the origins of cancer and have led directly to the concept of tumour suppressor genes.

Perspectives in Neuroscience Research: An Interview with Corey S. Goodman, Ph.D

In late October, Dr. Goodman visited Toronto as one of the winners of the 1997 Gairdner Awards. During this time, Neil Fam had the opportunity to interview him. Here, Dr. Goodman shares his views on the direction of neuroscience and the impact of molecular genetics on medicine.

News & Views: How did you first get into research and were there any early influences or role models?

Corey Goodman: I think I've been interested in science since I was a kid. I've always had a real interest in research and just trying to understand the mysteries of nature. When I went to college, I knew I wanted to have a life as a biologist. I did a whole variety of different research projects in a number of different labs as an undergraduate, and I felt I was searching around for what I was going to find interesting. Then in my junior year as an undergraduate, I took a neurobiology course by a professor named Donald Kennedy. I was a very shy student who would never go and talk to professors or quibble about exams. But I went to go see this professor to ask him if I could take his graduate lab course. Little did I know that a term paper I had written for him, which had come back with an A, he had thought was just superb and had been raving about it to his grad students. He instantly said that "sure," I could take his lab course and do research in his lab and, actually, it's been a lifelong relationship. There have been a lot of wonderful courses I've taken, but that one stands out.

NV: What advice would you give someone just starting out to be successful in science?

CG: Finding something you love and having some passion for it. Find a problem that you're really curious about and you just want to crack it. Not everybody is going to start out having a problem that they are really interested in. At some point, something will turn you on. There are a lot of discoveries that come up in a serendipitous way. You see a lot of people jumping around. At some point, you find a problem and you just take that challenge. You say, "I'm going to figure that out." It's fun, and everything in your life should have that sort of passion to it. If you're happy you hope that your personal life has it and you hope your professional life has it.

NV: The 1990s have been called the decade of the brain. As we approach the end of the decade, can you share your perspectives on where we are now and where this field might go in the future?

CG: Right now, people are using molecular biology and genetics to look at genes and at the proteins they encode one at a time. We tend to be reductionists. We take things away and we add them back. That's very powerful. But of course, in the real cell, things aren't working one at a time. They're intermeshed in networks of other gene and protein functions. So we're all looking at moving towards studying how networks of molecules are interacting. What we're waiting for is new levels of resolution to be able to watch in real time how information is processed in the brain. There are imaging methods now, but they're not quite there. I think that over the next decade, we'll begin to see, both at the molecular and cellular level, new techniques that let us see how many genes, proteins or cells are functioning at once.

That's going to be the level that you start understanding how the brain works.

think this is going to happen within the next year, but perhaps within the next decade.

NV: Although the function of individual neurons, and even sets of neurons, is beginning to be understood, the emergent properties of large populations of neurons such as emotion, consciousness and personality are more enigmatic. Will we ever achieve a complete understanding of the human brain?

CG: I think the answer is yes. I've heard people debate that the brain can't understand the brain. I don't buy those arguments. I think it's going to require new techniques to image the brain and lots of computational ability because we're going to be inundated with huge amounts of information. We're going to need ways to extract patterns from that data. I think that in a lot of fields of biology, including neuroscience, there is going to be a real future for people who have not only knowledge about biology, but also knowledge of computer science.

NV: Research on spinal cord injury has received lots of media attention. Is spinal cord regeneration a possibility and if so, what is the time frame?

CG: Certainly it is a possibility. In principle there is no reason why someday, we shouldn't be able to get the spinal cord to regenerate. There was a point back in the 1980's where we thought there was something we could sprinkle in to make the spinal cord regenerate, for example some sort of growth factor. But then came the insight that perhaps it wasn't just the absence of something positive, but the presence of something negative that prevents spinal cord regeneration. What wires the nervous system in the first place is a balance of attractive and repulsive signals. During development, cells are simultaneously being pushed and pulled along. Maybe some of those negative factors persist into adult life. We might ask why, and why aren't they present in a frog or a fish? No one knows for sure, but you can imagine that our nervous system is much more complicated and we have more plasticity than lower organisms. One theory would be that in order to allow all the sprouting and dynamic changes that take place in the nervous system, but to prevent miswiring, we've left a lot of these repellents and inhibitors peppered all over the nervous system to hold the basic wiring in place. For spinal cord regeneration, the final solution will likely be a cocktail of both inhibitors of the inhibitors and some extra growth stimulators. You probably don't need 100% of the connections to reform, as the human nervous system is very plastic. If people just get a little function back to motor neurons and pattern generators, through experience they can strengthen, modify and fine tune those connections. With respect to time frame, I don't

NV: Molecular research has had a tremendous impact on the field of medicine, for example, the cloning of disease genes, the genome project and our understanding of development. This trend promises to continue. Where do you see medicine in 30 years?

CG: We're going to know a lot more about the fundamental process of disease. Disease can be caused by genetic alterations, as well as environmental insults. But those environmental insults usually tend to be working through common biochemical pathways. Through genetics, you can identify key molecular steps that cause disease, which opens up knowledge about biochemical pathways. Ultimately, that can give you an idea about how many different kinds of factors can lead to the same disease, because ultimately they are impinging on the same biochemical pathway. For example, in Alzheimer's disease, we have the two presenilins that are highly related; although at the moment we don't know what they normally do, there is the chance now to find out what cellular process they are involved with and what's going wrong in the genetic forms of Alzheimer's. All of that knowledge, even if it only represents a subset of people with Alzheimer's, will teach us about the molecular biology of the disease and the biochemical pathway that's involved. We'll start to see different points that make that pathway go wrong, and I think suddenly, our approach to the disease will be to find nodal points in the pathway to intervene through drug discovery that will alleviate the disease. In addition, the incredible conservation of gene function in lower organisms such as *Drosophila* and *C. elegans*, all the way up to mammals and humans allows us to gain powerful insights into human disease through the use of these genetic model systems. I think we'll continue to find that many diseases have a genetic basis, either outright, or in terms of proclivity, something about your particular set of genes that makes you more or less susceptible. In terms of the way medical students are being trained today, when you think about what the genetic knowledge base is going to be 10 or 15 years from now, if I was thinking about becoming a doctor I would want to make sure I had a good understanding of basic genetics, because doctors are going to be making decisions and the information base will have a very genetic bent to it. And then there are lots of societal issues. We're going to see the day when different technologies will allow us to know at birth or before birth what our genetic proclivities are. It will be you guys, the future doctors, as well as politicians and others who will have to sort out how to use that information. But I think that's solvable and the exciting part is that we're going to have a much better idea about how to cure disease.

A Pair of Paralytic Punctures

Denise Campbell, Ph.D (OT0)

Presentation of Case

A fifty year old married man, Mr. V., was admitted to hospital with a 5 month history of progressive ataxia.

Mr. V. was well until six months prior to admission when he had a fever for four days. Over the next several months he experienced increased difficulties with walking and balance, and he complained of throbbing pains in his arms and legs. Four months prior to admission the vision in his right eye became blurred. One month prior to admission Mr. V. had a CT of the chest which revealed a left hilar mass. At the time of his admission to hospital his mobility had deteriorated to the point of requiring two people or a wheelchair for assistance. Mr. V. experienced loss of appetite, and a weight loss of 25 lbs. over a six month period. He complained of difficulty eating because tremor caused him to bite his tongue. He also had intention tremor in both hands and numbness in both legs. Onset of leg numbness ascended the left leg and then descended the right leg. Mr. V. complained of new throbbing headaches, which improved when his Tylenol use was reduced. Sleeping difficulties and a depressed mood were complicating factors. He was afebrile at the time of admission.

Admission medications included thyroxine for a 6 year history of well controlled hypothyroidism, and Effexor (Venlafaxine hydrochloride) for anxiety. Mr. V. quit smoking 6 years ago, and he drinks alcohol occasionally. The family history was unremarkable. At the time of admission, physical examination revealed a normal precordial exam with no peripheral edema. Peripheral pulses were all pre-

sent. Breath sounds were normal and the abdominal exam was unremarkable. Mr. V. was alert and oriented. He had bilateral gaze evoked nystagmus and bilateral papilloedema. There was decreased vibration and position sense in both feet. The arm power was 4+/5 distally and all reflexes were normal (2+/4). He had truncal ataxia and required support to stand. In addition, Mr. V. had increased expressive speech difficulties and was reverting to his native Portuguese tongue with greater frequency. A right handed calligrapher, Mr. V. could not write at the time of admission. The lab results are presented in Table 1, and a summary of the imaging studies is shown in Table 2.

Table 1
Miscellaneous Laboratory Results on Admission

Test	Result
Liver function tests	Normal
Calcium	Normal
Protein electrophoresis	Normal
Angiotensin-converting enzyme (ACE)	Normal
Atrial natriuretic factor (ANF)	Normal
Erythrocyte sedimentation rate (ESR)	Normal

A bone scan demonstrated no scintigraphic evidence of metastatic disease. Salivary gland scintigraphy was performed as there was a past history of a benign Warthin's

tumor on the right side, and there was new parotid swelling on the left side. There was no scintigraphic evidence of a Warthin's tumor on the left side. Another CT of the chest was performed. A 2 cm mass was located posterior to the left upper lobe bronchus, apparently encasing the inferior pulmonary artery. A portion of the mass insinuated itself between the left pulmonary artery and the aorta. The increasing size of this mass during the interval between chest radiographs suggested a neoplasm. Further investigation to determine the etiology of the mass was arranged.

Table 2
Imaging Studies

Test	Result
Bone Scan	Normal
CT Thorax	Left hilar mass
Enhanced MRI of the head	Small lacunar infarcts bilaterally in the head of the caudate nucleus
Salivary Scan	Normal

A CT-guided needle biopsy was performed. There was an unexpected complication of the procedure. There was extensive discoloration of the left posterior chest wall which was initially thought to be a hematoma, but was subsequently shown to be a 30 cm wheal. This was postulated to be a reaction to the local anaesthetic and 50 mg i.v. of benadryl were administered. Mr. V. was asymptomatic and was returned to the floor for observation.

On awakening the next morning, he was unable to move either of his legs and he had urinary incontinence. The temperature was 38°C and there was no neck stiffness. Peripheral pulses were all present, the calves were not swollen, and there was fair capillary refill. Deep tendon reflexes were 2+ in both arms, and were 0 in both legs. There was no anal wink, decreased sphincter tone and an increase in the amount of stool in the rectum. Power was 4 in both arms and 0 in both legs. Vibration sense was present in both legs, but was decreased bilaterally. Sensation of pin prick was reduced below T8.

A CT myelogram of the total spine was normal as there was no obstruction to the flow of contrast throughout the spine, with no evidence of extradural, intradural, or intramedullary masses. A magnetic resonance image (MRI) of the head was performed and there were no areas of abnormal contrast enhancement and no abnormalities were identified. The previously noted abnormalities within the caudate nuclei bilaterally were not well demonstrated on the sequences used in this exam. Repeat chest x-rays were performed on the day of the fine needle biopsy and the following day. Both x-rays revealed a small left apical

pneumothorax with the visceral pleura projected at the level of the posterior third rib secondary to the biopsy procedure. A lumbar puncture was performed and the results are included in Table 3.

Table 3
Lumbar Puncture Results

Test	Result
Protein	3.6 g/L increased
IgG	0.79 g/L increased
WBC Counts	61 x 10 ⁶ /L
Flow Cytometry (CD45, CD2, CD19)	Mainly T lymphocytes
Glucose	Normal



FIGURE 1. MRI of the Spine. (no contrast, T2 weighted)

Over the following few days the patient's speech became more audible, there was increased tone in both legs, and the deep tendon reflexes returned to 2/4. There were no Babinski reflexes. Mr. V. was unable to move his legs voluntarily, and his indwelling Foley catheter remained in place. An MRI of the spine was performed 8 days following the fine needle biopsy and the results are shown in Figure 1.

Radiologist's Comments

There is an abnormal increase in signal intensity within the central spinal cord which extends from T4 to T8 (arrow). The spinal cord cephalad to T4 is normal in contour and signal intensity, as is the spinal cord caudad to T8. There is no expansion of the spinal cord throughout. The spine is otherwise normal in appearance. There is no evidence of intra- or extradural lesions, nor is there any evidence of spinal stenosis.

The CT-biopsy sample obtained was unfortunately not diagnostic. The suspicion was that the small cells obtained were more consistent with lymphoma than with small cell lung cancer (SCLC). The patient was started on decadron to attempt to shrink the mass. A tuberculin skin test was negative, and a mechanical lesion below T1 was ruled out.

Two weeks following the attempted biopsy, Mr. V. was able to move his quadriceps muscles bilaterally, as well as his right gastrocnemius. He had normal power in his arms, and he had no difficulties speaking. As the previous biopsy was uninformative, it was necessary that the procedure be repeated. The lesion was not amenable to other approaches. Two days later the CT-guided needle biopsy was repeated. Prior to the procedure the patient was given benadryl, valium, and morphine. The patient tolerated the procedure well, with a small pneumothorax remaining and no evidence of a skin reaction. He returned to the floor for observation. The biopsy results showed abnormal cells consistent with anaplastic SCLC. Immunohistochemical stains were positive for low molecular weight keratin, and negative for leukocyte common antigen.

Approximately two hours following the biopsy procedure, Mr. V. became confused and had expressive aphasia. He experienced sudden right arm weakness. The BP was 130/100 in both arms, pulse was 114 and regular, and he was afebrile. Pupils were reactive to light with consensual reflexes. The right pupil was larger than the left pupil. The patient had right homonymous hemianopia. Extraocular movements were not consistent in tracking into the right visual field. There was no facial droop. Cranial nerves V, VII, VIII, XI, and XII were not testable, although he did have a corneal reflex. Mr. V. had a gag reflex and he could swallow. There was a normal doll's eye sign, except that horizontal nystagmus was elicited. The sensory exam was grossly normal in all limbs. He responded to right arm pain by localizing with his left arm. He had mild global hyperesthesia. On examination Mr. V. had a flaccid right arm, with normal tone and normal reflexes in the left arm and legs. There was no Babinski sign. Motor power was

0/5 in the right arm and both legs, and it was normal in his left arm.

A CT without contrast of the head was performed and compared with one done three weeks before. There was no evidence of infarction and no hemorrhage. The degree of cerebral and cerebellar atrophy was considered out of keeping with his age. Four days later a CT with contrast was performed. Again there was no evidence to suggest a recent infarction, nor was there any evidence of metastatic disease. Over that same period Mr. V. had a urinary tract infection and was treated with septrin/pyridium. His speech improved over this period. Although he was unable to move his right hand and arm, he was able to dorsiflex his right ankle, move his left foot, and flex his left quadriceps muscle.

Twelve days following the second fine needle biopsy Mr. V. was started on chemotherapy with etoposide (VP-16) and carboplatinum which he tolerated well. Six days later he presented with chest pain and was diagnosed with pulmonary emboli on the basis of a V/Q scan, for which he was successfully treated.

Two weeks later Mr. V. was treated with radiation therapy (1895 cGy external beam radiation) to the primary lesion in the mediastinum. The rationale for the treatments was the possibility of marginally increasing survival, and improving local control of the tumour. One month following the initial chemotherapy treatment, and in the middle of the radiation therapy course, Mr. V.'s neurological condition improved as he was able to move his arms and legs, and he had increased bladder sensation. He was discharged from hospital four days following the end of his radiation therapy treatments. He went on to have three further cycles of chemotherapy. His clinical situation remains stable and unchanged six months following his discharge from hospital.

Differential Diagnosis

The differential diagnosis of an enlarging mediastinal mass includes both malignant and non-malignant etiologies. The malignant causes include SCLC, non-small cell lung cancer, lymphoma, mediastinal germ cell tumour, and a metastatic carcinoma of an unknown primary. The non-malignant causes include sarcoidosis, histoplasmosis, and tuberculosis.

A normal ACE is suggestive against sarcoidosis and the normal ANF helps to rule out collagen-vascular disease. ESR is non-specifically elevated during inflammation and a negative result reduces concern of an underlying inflammatory process. Abnormal liver function tests would cause concern about possible hepatic metastases, although normal results do not rule out the presence of metastases. The normal protein electrophoresis suggests against multiple myeloma and low grade lymphoma. As well, the immunohistochemistry of the biopsy sample was negative for leukocyte common antigen which suggests against a lymphoid neoplasm.

A diagnosis of anaplastic SCLC was made. In the absence of an obvious disease process in the cerebellum and the presence of SCLC, the progressive neurological problems are consistent with paraneoplastic cerebellar degeneration (PCD). PCD is the first issue of discussion in this case.

Paraneoplastic syndromes are defined as disorders of host function occurring at a site remote from the primary tumor or its metastases.¹ Carpentier and Delattre (1996) defined neurological paraneoplastic syndromes as an association between neurological disease and cancer in the absence of metastatic, infectious or metabolic disease.² The incidence of paraneoplastic syndromes is ~1% of all cancer patients, and ~3% of lung cancer cases.³ In cases of neurological paraneoplastic syndromes, encephalomyelitis occurs in approximately 80% of these cases, followed by brain-stem encephalopathy (30%), limbic encephalopathy (20%), motoneuron dysfunction (20%), paraneoplastic cerebellar degeneration (15%), and autonomic neuropathy (10%).³

Encephalomyelitis is an inflammatory disorder which can affect one or several levels of the nervous system. The level affected determines the clinical findings as summarized by Dalmau and Posner (1997).⁴ Encephalomyelitis usually follows a subacute course and it is frequently disabling. It often occurs with occult malignancy, frequently SCLC, and there is no known cure. At the initial stages there is cerebrospinal fluid (CSF) pleocytosis and there is an increase in CSF protein and IgG. The anti-Hu antibody is commonly found.⁴

Table 4
Encephalomyelitis: Clinical Findings at Different Levels of Nervous System Involvement

Nervous System Level	Clinical Findings
Muscle	myositis
Sympathetic Nervous System	orthostatic hypotension
Parasympathetic Nervous System	intestinal pseudo-obstruction, urinary retention
Peripheral Nerve	sensorimotor neuropathy, neuromyotonia
Dorsal Root Ganglia	sensory neuronopathy
Spinal Cord	transverse myelopathy, motor neuronopathy
Brainstem	opsoclonus, vertigo, hearing loss, ocular palsies
Cerebellum	paraneoplastic cerebellar degeneration
Limbic System	amnesic dementia

Adapted from Dalman and Posner (1997).⁴

PCD is a neurological paraneoplastic syndrome which is characterized by the subacute development of severe pancerebellar dysfunction. This dysfunction is associated with the loss of Purkinje cells, and occasionally with meningeal and deep cerebellar nuclear inflammatory infiltrates.⁵ PCD occurs in less than 2% of cancer patients.³ The three most commonly associated forms of malignancy are lung cancer, ovarian cancer, and Hodgkin's disease.³

Three different antibodies may be present in some of the patients with PCD. These antibodies are important as each is associated with different malignancies. The presence of the anti-Yo antibody is observed with ovarian and breast carcinoma, the anti-Hu antibody is characteristic of SCLC, and the anti-Ri antibody is found in SCLC or breast carcinoma.³

In this case there was a reasonable index of suspicion, which was later confirmed, that the lung mass could be neoplastic. Inflammatory changes of the CSF are observed in many patients with PCD.⁵ In this case, there was an increase in CSF protein, IgG, and CSF pleocytosis (Table 3). Anti-Hu and anti-Yo antibodies were requested by the medical staff, but the results were not obtained by the laboratory. The anti-Hu antibody test was done eight months later, and was negative in this patient. This result does not rule out PCD.

PCD is a disabling neurological condition which does not usually respond to treatment.⁵ In a few patients, corticosteroids/immunosuppression or plasmapheresis have been of some benefit.^{3,5}

The second issue in this case concerns the neurological difficulties following the initial biopsy procedure. The diagnostic possibilities include transverse myelitis or a vascular disorder such as acute anterior spinal artery syndrome. According to the radiologist, the absence of expansion of the spinal cord contour makes acute demyelination an unlikely possibility for this appearance.

The clinical impression was that the patient was suffering from acute spinal shock, likely due to a compromise of the anterior spinal artery. The dorsal columns were relatively preserved, thus perfusion of the posterior cord was adequate.

Most spinal cord infarctions are due to distant vascular occlusions or to severe hypotension⁶. Infarction can be caused by interruption of the radicular and/or direct arterial supply to the anterior and posterior spinal arteries.⁶ The watershed region of the thoracic cord is between the anterior spinal artery where it arises from the vertebral arteries, and the artery of Adamkiewicz, which is the large tributary arising off the lower aorta.⁶ The watershed region is frequently affected in spinal cord infarctions.⁶

Mr. V. was not noted to be severely hypotensive during the procedure. The location of the biopsy at the level of the posterior third rib indicates that the allergic reaction experi-

enced during the first biopsy may have caused constriction of the vertebral arteries. These vessels enter the intervertebral foramina to join with the anterior spinal artery, and their occlusion may have impeded blood flow to the anterior spinal artery.

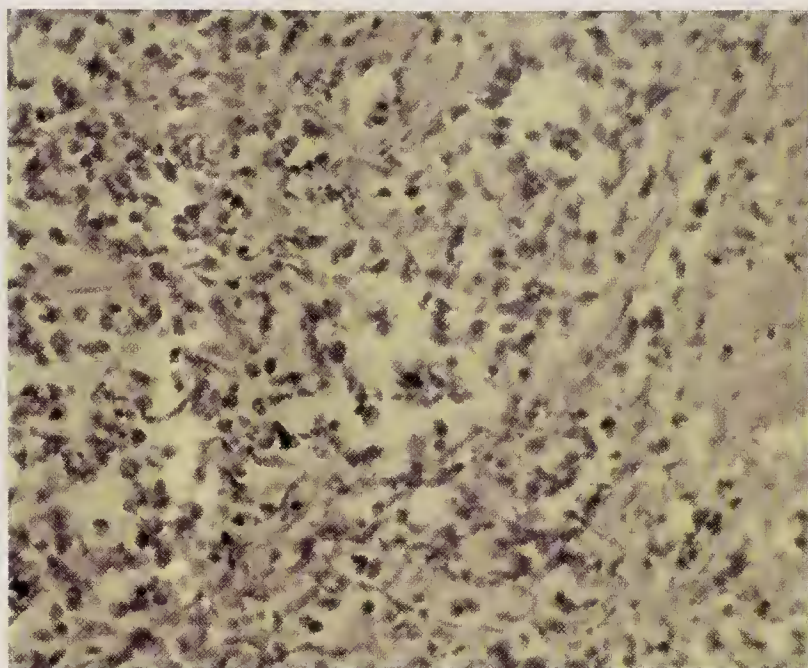


FIGURE 1. Small Cell Lung Carcinoma.
Note the small darkly staining tumour cells with scant cytoplasm.

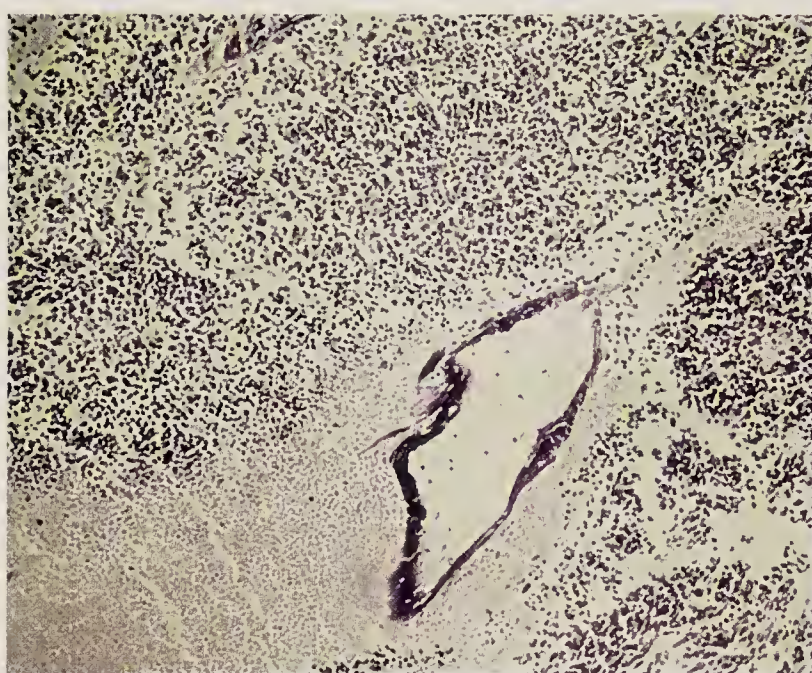


FIGURE 2. Small Cell Lung Carcinoma.
Note the basophilic outlining of the blood vessel wall.

The inflammatory reaction alone may have been sufficient to trigger the infarction. There have been reports of spinal infarction secondary to inflammatory processes including serum sickness, systemic arteritis, and following intravascular contrast injection (with severe back pain at time of injection).⁶

As seen in Table 4, encephalomyelitis at the level of the spinal cord (necrotizing myelopathy) can result in transverse myelitis. Necrotizing myelopathy presenting as subacute transverse myelitis, frequently in a thoracic location, is a rare complication of malignancy.⁷ The clinical findings include leg and arm paresis, sensory loss, and urinary bladder sphincter problems.⁷ The increases in CSF protein and cell count seen in severe cases of necrotizing myelopathy are consistent with this case. However, there was no spinal cord swelling observed. Spinal cord swelling is a feature of some severe cases of necrotizing myelopathy.⁷ Initially, Mr. V. may have had subacute spinal cord involvement as he complained of throbbing pains in his arms and legs, and asymmetric paresthesias in the legs. The acute allergic reaction following the first biopsy may have been able to trigger acute transverse myelitis.

The third issue in this case are the neurological complications arising from the second biopsy. These events are consistent with an embolic stroke involving the left middle cerebral artery territory. Possible triggers include non-bacterial thrombotic endocarditis (the most common cause of stroke in cancer patients), or a cardiac source such as atrial fibrillation after the procedure. There was no radiologic evidence of a stroke immediately following the event or four days later. CT scanning is not always perfectly sensitive to the presence of infarction, especially in the first few hours.

Diagnoses

Anaplastic Small Cell Lung Carcinoma with Paraneoplastic Cerebellar Degeneration

Pathological Discussion: Small Cell Lung Cancer

Small cell lung carcinoma (SCLC) is seen typically as a central lesion developing around a major bronchus. The lesion often extends into the adjacent parenchyma and often presents with diffuse, extensive mediastinal metastases. Commonly, SCLC grows and spreads along submucosal lymphatics causing the mucosa to become diffusely thickened and roughened. Erosion of the mucosa and bronchial compression may occur. The tumour is soft, grey white and shows myxoid degeneration. Areas of necrosis and hemorrhage are often present.⁸

On histological appearance, usually SCLC cells have dark, hyperchromatic ovoid nuclei with dispersed chromatin patterns and inconspicuous nucleoli. The cytoplasm is barely visible and cells are approximately twice the size of a normal lymphocyte.⁸ The cells are shown in Figure 1. Other morphologies are also possible. The tumour cells grow in uniform sheets or as anastomosing trabeculae separated by connective tissue stroma with focal areas of necrosis. DNA from necrotic tumour cells cause a characteristic basophilic outlining of blood vessel walls as shown in Figure 2. Usually neither a desmoplastic response nor significant inflammatory infiltrates are observed.

Electron microscopic studies reveal dense-core neurosecretory granules in some tumour cells. The granules are similar to those found in neuroendocrine cells present along the bronchial epithelium and betray the probable neuroendocrine origin of SCLC.⁸

SCLC is sensitive to radiation and initially to chemotherapy. Multidrug resistance is a major complication of treatment. This cancer is the most metastatic of all lung tumours. The mean survival after diagnosis with SCLC is about one year.⁸

Conclusion

Mr. V. is a 50 year old man with SCLC and PCD. The unusual features of his case were the vascular sequelae to the two CT-guided needle biopsies performed to diagnose his mediastinal mass, and his apparent improvement in neurological function following treatment. Mr. V. is stable sixteen months following the onset of symptoms of PCD.

Acknowledgements

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When the Best Defense is a Good Offense

Steven Shumak MD, FRCPC* and
Jonathan P. Gladstone, BSc. (OTO)

Introducing Morning Report

Morning Report Rounds are challenging and stimulating daily exercises in teaching hospitals throughout North America^{1,2}. In each issue, *Morning Report* will try to capture the unique dynamics of *Morning Report Rounds* by focusing on the clinical decision making process of a real case from a University of Toronto teaching hospital. A clinician involved in the patient's care will provide a running commentary of the case to emphasize various components of the clinical reasoning process: reviewing the pertinent positive and negative features of the history and physical examination; generating diagnostic hypotheses; anticipating laboratory findings; weighing the evidence to rule in or rule out the differentials; and discussing patient management. The goals of *Morning Report* are to demonstrate how an expert clinician "thinks through" a case from the presenting symptoms to the final diagnosis, and to exemplify the management of common, important medical and surgical disorders.

Anyone wishing to pose questions, challenge issues raised, or elaborate on personal experience in similar scenarios, please contact this e-mail address, jon.gladstone@utoronto.ca. We also invite any clinician who has a case of educational value and who is interested in collaborating with the *UTMJ* to contact The Editor at the same e-mail address.

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Jennifer Bosy

Presenter: A 54 year-old man came to the Emergency Department complaining of a twelve hour history of chills and fever to 39.3°C. He had been in his usual state of health until the evening of presentation when he began to feel generally unwell. At that time, he began to develop shaking chills and noted that his temperature was elevated.

The patient was known to have longstanding mitral valve prolapse with mitral regurgitation and had been treated 18 months previously for an episode of infective endocarditis due to *Streptococcus viridans*. He had been told by his doctors to come to the Emergency Department promptly should he ever develop a fever. He therefore presented to the ER at this time.

Dr. Shumak: I am surprised this man's mitral valve was not replaced after his episode of endocarditis. Regardless, we have already reached a "break point" in this man's case. We will have to decide whether he has developed another episode of infective endocarditis, or whether he has one of the many other causes of fever.

P: Perhaps you could provide a brief overview of infective endocarditis before we proceed further.

Dr. S: Infective endocarditis refers to an infection of the valvular endocardium, usually by bacteria but occasionally by non bacterial micro-organisms. Very often, there is an underlying valvular abnormality which predisposes to the development of endocarditis. Presumably, this abnormality leads to turbulence of blood flow with subsequent endocardial damage at the site of the turbulent jet. Platelets and fibrin tend to adhere to such sites and may become infected during bacteremias.

In the pre-antibiotic era, infective endocarditis was always fatal. Even today, it carries with it significant morbidity and mortality. The infective process may destroy the infected valve and lead to refractory congestive heart failure. In addition, aggregates of fibrin, platelets and micro-organisms (i.e. vegetations), form on the infected valve. Should these vegetations dislodge, the result will be embolization. Depending on the site of embolization, the consequences can be catastrophic.

Clinically, infective endocarditis has been divided into two types – subacute and acute. Subacute bacterial endocarditis (SBE) typically occurs insidiously and presents with symptoms of chronic disease (i.e. with constitutional symptoms) whereas acute bacterial endocarditis (ABE) has a more well defined onset often associated with a very high fever. Both types may be complicated by the development of emboli.

It is important to note that the microbiologic causes of SBE differ from those of ABE. In non-intravenous drug users, SBE most commonly results from *Streptococcal* infection, usually *S. viridans*, and ABE is most likely to be

caused by *S. aureus*. In addition to requiring different antibiotic regimens, the two types of endocarditis differ in the likelihood that surgical intervention will be required. Frequently, ABE has such a fulminant course that surgery must be undertaken before medical therapy has any chance to succeed.

P: How would you approach this case?

Dr. S: I would like to know at the outset whether this man has had any risk factors for the development of endocarditis such as recent dental work, or bowel or bladder instrumentation. I would want to know without delay whether there are obvious clues to guide us to alternative explanations for his fever such as coryzal symptoms, or those of a simple viral gastroenteritis.

P: The patient had no coryza, cough, sputum, diarrhea, dysuria, or urinary frequency. He has no known drug allergies.

Dr. S: No obvious alternative explanations for this man's fever are apparent. This further increases our index of suspicion for endocarditis.

P: Five weeks previously, the patient had undergone dental cleaning with Amoxicillin prophylaxis.

Dr. S: The use of Amoxicillin prophylaxis was appropriate and would provide adequate coverage for most oral micro-organisms associated with infective endocarditis. Even though there is no proof of its efficacy, antibiotic prophylaxis is an accepted standard of practice in an individual with known underlying valvular heart disease undergoing a procedure which might result in a bacteremia. However, the vast majority of individuals with infective endocarditis do not have the classic antecedent risk factors for infectious endocarditis such as dental extractions or genitourinary (GU) instrumentation. The simple act of brushing one's teeth is associated with significant rates of bacteremia and bacteremias also occur spontaneously. Given these facts, it is remarkable that infective endocarditis is not ubiquitous in people with valvular heart disease. It is estimated that no more than 5-10% of cases of infective endocarditis are preventable even with appropriate antibiotic prophylaxis.

P: The patient had recently been diagnosed with obstructive sleep apnea and had been using Continuous Positive Airway Pressure (CPAP) for approximately one week.

Dr. S: I am unaware of any association between CPAP use and infective endocarditis. It seems plausible that the positive pressure might disrupt the normal barriers to bacterial invasion in the nasopharynx. However this is speculation. One could speculate further that any

micro-organisms entering the circulation in this way would reflect the flora of the nasopharynx and might, therefore, include *S. aureus*.

P: What else would you be looking for on a focused history?

Dr. S: In this man with known valvular heart disease and a history of infective endocarditis, once we consider endocarditis, we are obligated to look for its symptoms and signs. Accordingly, I would ask about symptoms of embolism. Classic sites of embolism would include the brain (causing stroke-like symptoms), the spleen (causing flank pain), the kidneys (causing both flank pain and hematuria), and the skin itself. In the latter instance, the patient or the physician may notice painless or painful non-blanching erythematous lesions especially on the distal extremities. There is also some overlap here with a serum sickness-like process which can develop as the result of the formation of an IgM anti-IgG antibody

which occurs as a result of the ongoing bacteremia. It would also be important to search for further evidence of complications of infective endocarditis such as congestive heart failure. I would want to know whether he is experiencing shortness of breath, orthopnea, or chest pain.

P: There were no symptoms to suggest congestive heart failure, nor were there any symptoms of stroke, flank pain, abdominal pain, or hematuria. What would you look for on physical examination?

Dr. S: The physical examination will be important. Many clues to infective endocarditis or other cause of this man's fever may be found. I would pay close attention to his skin and the cardiac system.

P: His temperature was 37.6°C, respiration rate 18 breaths/min., heart rate 80 bpm and regular, and BP 105/60. His JVP was not increased and no crackles or extra heart sounds were present.



a. Left thumbnail



b. Sole of right foot



c. Palm of left hand



d. Left elbow

FIGURE 1. Cutaneous manifestations of infective endocarditis

The lesions in the a) left thumbnail, b) sole of right foot, c) palm of left hand and d) left elbow, are consistent with embolic phenomena from infective endocarditis. The lesions on the palm and sole are highly suggestive of Janeway lesions.

Dr. S: Congestive heart failure seems unlikely given these findings.

P: There was a III/VI pansystolic murmur heard at the cardiac apex with prominent radiation to the axilla. The murmur was felt to be compatible with his known mitral regurgitation. On dermatologic exam, there were two splinter haemorrhages on the distal left thumb nail that were longstanding according to the patient. He also had a single, new, non-tender petechial-looking lesion on the sole of his left foot.

Dr. S: The cutaneous manifestations of infective endocarditis are often searched for and seldom found.

P: Perhaps you could review them for a moment?

Dr. S: There are at least three classic cutaneous manifestations of infective endocarditis: splinter haemorrhages; Osler's nodes and Janeway lesions. Splinter haemorrhages are linear haemorrhages in the nail beds whose axes are parallel to the long axis of the finger. To the eye, they appear deep brown or black. Distal thin splinter haemorrhages are likely due to trauma. Wider and more proximally located splinter haemorrhage are more likely to be of pathologic significance. As with all of the classic manifestations of infective endocarditis, the true prevalence of splinter haemorrhages is impossible to ascertain. They are said to be less common in ABE than in SBE.

Osler's nodes are tender, red or purple subcutaneous nodules typically appearing on the palms or soles. Janeway lesions are non-tender, purpuric or erythematous macules also most commonly found on the hands and feet. Actually, the distinction between Osler's nodes and Janeway lesions may be an academic exercise (no less an authority than Sapira states that "I cannot tell the difference between the two."³ Both have been shown due to an immune vasculitis (from the mechanism mentioned earlier) and both due to septic emboli. Once more, I am unaware of reliable data to estimate the true prevalence of these lesions in endocarditis, however, Osler's nodes are said to be more common in SBE than ABE, whereas Janeway lesions predominate in ABE.

P: What tests would you include in your initial work-up of this patient?

Dr. S: The patient appears haemodynamically stable. I am not concerned about the splinter haemorrhages because they are old and distally located. I am concerned about the lesion on the foot. We must pursue the possibility of infective endocarditis. I would be interested in his CBC to look for a leukocytosis and I would want to examine his urine. The presence of RBC casts in this setting

would be supportive of infective endocarditis (i.e. it would be consistent with the presence of an immune complex glomerulonephritis). I would also want to see his chest x-ray and electrocardiogram with the latter test to check for signs of heart block, which might indicate the presence of myocardial abscess formation. Blood cultures would be extremely important in this setting and should be undertaken without delay. I will want to do an echocardiogram, although I recognize in advance it will be difficult to interpret given that he is known to have severe mitral valve disease. In other words, with extensive valvular disease, especially myxomatous mitral disease, it may be impossible to ascertain the presence of valvular vegetations. The yield may be increased by performing a transesophageal echo (TEF).

P: He had an elevated WBC of $19.8 \times 10^9/L$, 19.1×10^9 of which were PMNs. His haemoglobin was normal. He had a mild thrombocytopenia. His creatinine was normal. Urinalysis showed 3+ red blood cells and RBC casts in his urine. There was 1+ proteinuria. His ECG was unchanged from that obtained previously. The chest x-ray was unremarkable aside from minimal cardiomegaly.

Dr. S: A normal haemoglobin argues against a chronic process in this man. That, and his new-onset fever suggests infection. I am also concerned given the results of his urinalysis. As mentioned, infective endocarditis is associated with an immune complex glomerulonephritis. Finally, the lesion on his sole may be of the Janeway type.

Now we have a conundrum. Here is a man at risk for infective endocarditis. He has already had one episode and now presents with symptoms, signs, and laboratory evidence all compatible with another episode of infective endocarditis. Definitive diagnoses requires positive blood cultures. Should we start antibiotics now or wait? If we give antibiotics now we may sterilize his blood and thereby prevent a secure diagnosis of infective endocarditis. Without a firm diagnosis, issues such as duration of antibiotic therapy are problematic. Conversely, if we withhold antibiotics he may deteriorate. His acute fever, the known valvular disease, the urinalysis results, and the lesion on the foot are all consistent with ABE - a medical emergency. If this is in fact the diagnosis, delay in antibiotic therapy could have dire consequences. Accordingly, I would treat him empirically with antibiotics now.

P: Antibiotics were not given at the time of his hospitalization. Twelve hours after his admission, the patient was noted to have multiple new cutaneous lesions (Figure 1). The lesion on his foot was painful; the others were not. The patient's temperature was 38.4°C and he looked unwell.

Dr. S: The cutaneous lesions are characteristic of infective endocarditis. The rapid appearance of so many lesions,

coupled with the “sick” appearance of the patient indicate that we are almost certainly dealing with ABE. As mentioned earlier, the infective organism in ABE is usually *S. aureus* and we should assume that this is the culprit here. This man is critically ill. *S. aureus* ABE has a poor prognosis and he will likely need surgery for valve replacement soon. The internist’s job here is to buy time until surgery. Ideally, the goal will be to administer sufficient antibiotics to pre-operatively sterilize the valve and blood and avoid placing the prosthetic valve into the site of an active infection. In practice, the complications of *S. aureus* ABE such as systemic embolism, congestive heart failure, and myocardial abscess, may force our hand sooner.

I would start this man on vancomycin and gentamicin for presumed *S. aureus* endocarditis. I would use vancomycin in case the *S. aureus* was “methicillin resistant” and add gentamicin for synergy. As mentioned, this man is sick and may well die. We cannot afford to make any other mistakes. The cardiovascular surgeons need to be involved in this man’s care as he will surely need his valve replaced at some point. It is hoped we will be able to delay this as long as possible and minimize the chance of placing a new valve into a septic host.

P: Three of the three sets of blood cultures were positive for *S. aureus*. A TEE showed severe mitral regurgitation with a flail mitral valve. The study was technically difficult and it was impossible to determine if vegetations were present. His left ventricular function was normal. How should this patient be managed?

Dr. S: The positive blood cultures, the presence of an abnormal mitral valve, the presence of embolic phenomena (the cutaneous lesions), and fever have proved the diagnosis of infective endocarditis beyond doubt in this case. Now that we have instituted appropriate antibiotic therapy, he will need supportive care and monitoring. His ECG should be followed on a regular basis to check for the development of heart block which could indicate intramyocardial spread of the infection, or an abscess formation in the conducting system. He should also have blood cultures followed to ensure that they have become negative. He will need careful observation to check for the development of any symptoms or signs to suggest congestive heart failure. Refractory heart failure would be a clear indication for urgent surgical intervention. Likewise, should he develop major or recurrent systemic emboli, he would likely need surgery.

P: Approximately 36 hours after admission, the patient was afebrile but began to experience intermittent left sided chest pain. He described the pain as a deep burning and pointed to the area of his left nipple. The pain was not affected by breathing and there was no associated shortness of breath. The physical examination was unchanged. What possibilities come to mind?

Dr. S: Has he developed septic pericarditis due to rupture of a myocardial abscess into the pericardial space? Has he had a vegetation embolize to a coronary artery and is he now having angina or a myocardial infarction? In addition, I would have to wonder about all the other myriad causes of chest pain in a hospitalized patient with systemic sepsis. I would want to get an urgent ECG, chest x-ray, and 2-D echo.

P: The chest x-ray was unchanged from that obtained at admission. The 2-D echocardiogram showed no pericardial effusion. The ECG showed diffuse ST-segment changes but more pronounced inferolaterally. What does this suggest?

Dr. S: The diffuse changes you describe on the ECG are suggestive of pericarditis but the echo shows no effusion. More importantly, the ECG changes, while widespread, are not truly diffuse. Rather, we are told that they are most pronounced at two sites defined by their vascular supply, i.e. inferior and lateral wall. I believe this man has had an embolism to one of his coronary arteries, perhaps to the circumflex. I would try to get an urgent cardiac catheterization at this time. If there is evidence of coronary emboli, I think he should go straight to surgery for the dual purposes of dislodging the embolus and urgent mitral valve replacement.

P: He underwent urgent coronary angiography. The coronary arteries themselves were normal, but in the proximal circumflex there was a mobile obstruction compatible with an embolic structure. Cardiac surgery was performed on an urgent basis. The circumflex artery was flushed and an embolectomy catheter passed. The left atrium was described as “huge.” Both mitral valve leaflets were grossly infected and requiring total excision, and subsequently replaced with a mechanical mitral prosthesis. The excised valve tested positive for gram positive cocci, consistent with *S. aureus*.

Dr. S: We are not yet out of the woods. First, we have placed a mechanical valve into an infected host. He will need at least an additional six weeks of parenteral antibiotic therapy. Second, although the circumflex artery is now patent, he may have already had a myocardial infarction. Third, the presence of a mechanical heart valve obliges the use of life long anticoagulation.

P: On the first post-operative day, sensitivity assays show that the *S. aureus* was sensitive to cloxacillin. Accordingly, the vancomycin was stopped and cloxacillin started. The gentamicin was continued.

Post-operatively, the patient's creatinine began to climb as indicated in the following table:

POST-OPERATIVE DAY	CREATININE (mmol/L)
0	100
1	152
2	139
3	194
4	194
5	N/A
6	225
7	265
8	343

P: What are the potential etiologies of this man's renal dysfunction?

Dr. S: There are a number of explanations, including: the evidence of an active glomerulonephritis upon admission to hospital (i.e. the RBC casts in the urine); his exposure to nephrotoxic agents (vancomycin, gentamycin and the angiogram dye); finally, his endocarditis places him at risk for renal embolization. The list of possibilities continues and includes possible intra-operative hypotension leading to acute tubular necrosis (ATN) or even his initial septic episode culminating in ATN. Finally, the cloxacillin could be causing an interstitial nephritis on an allergic basis.

P: How would you approach this problem?

Dr. S: At this time, the physical exam should be repeated and a search made for signs of volume depletion as well as for fever or other evidence of a hypersensitivity reaction. Laboratory testing would include serum electrolytes, especially potassium and bicarbonate, a urinalysis and a urine sodium level. A urine culture should also be sent. The urinalysis may help us determine whether he has an active glomerulonephritis still ongoing and the urine sodium would give us some indication whether we are dealing with a pre-renal or renal cause of his problem. I would also test his urine for eosinophils to help diagnose an allergic response to the cloxacillin which, as mentioned, could be causing an interstitial nephritis. I assume that his gentamicin levels had been followed and the dose was adjusted appropriately. Regardless, I would discontinue the gentamicin at this juncture. We should try to eliminate all unnecessary potentially nephrotoxic drugs. He needs a Foley catheter if one is not already in, as well as an abdominal ultrasound to check for post-renal obstruction. After all, he is a middle aged man who has been in the hospital for some time and may simply have developed manifest prostatic obstruction.

Often in complex cases like this, no single cause for the renal insufficiency can be identified. Instead, the decline

in renal function may be attributed to multiple etiologies. In the absence of a clearly defined cause, the clinician must revert to basic principles and ensure that there is adequate pre-load to the kidney (i.e. maintain the volume), ensure there is no obstruction to urine flow, treat any infection, and avoid nephrotoxic drugs and agents. All the while, the clinician must continue to treat the underlying or associated systemic diseases.

P: The gentamicin had been stopped on post-operative day four when the creatinine was 194 mmol/L. Prior to that, the levels were therapeutic. The physical examination showed that his JVP was 2 cm with no orthostatic changes in his BP or pulse. The abdominal ultrasound showed no post-renal obstruction. The potassium and bicarbonate were normal. The urinalysis showed 15-20 WBC/HPF, 10-15 RBC/HPF, many heme granular casts and also WBC casts. There was 1+ proteinuria. His urine sodium was 50 mM/L. The urine culture was negative. The urine stain for eosinophils was negative.

Dr. S: He appears euvolemic and there is no evidence of obstruction. The urine is sterile. The urine sodium of 50 mM/L indicates established renal disease as opposed to a strictly pre-renal problem where one would expect the urine sodium to be much lower, usually less than 20 mM/L. The heme granular casts are non-specific but are certainly consistent with ATN of multiple etiologies. On the other hand, the WBC casts raise the possibility of acute interstitial nephritis and renal infection. However, as noted, his urine is sterile. The fact that his urine is negative for eosinophils should not dissuade us from considering the diagnosis of acute interstitial nephritis. The test is not sensitive and, in this case, the prior probability of acute interstitial nephritis is high.

Nevertheless, I would default to probability and favour ATN as the explanation for this man's renal dysfunction. In other words, ATN is common and clearly could have followed the gentamicin use, the radiocontrast dye that he received, the initial septic episode, or even simply the cardiac surgery itself. I am also impressed by the heme granular casts which should not occur in uncomplicated acute interstitial nephritis. There is no specific therapy for ATN. Rather, we support the patient and try to do no harm. Dialysis is not yet on my mind.

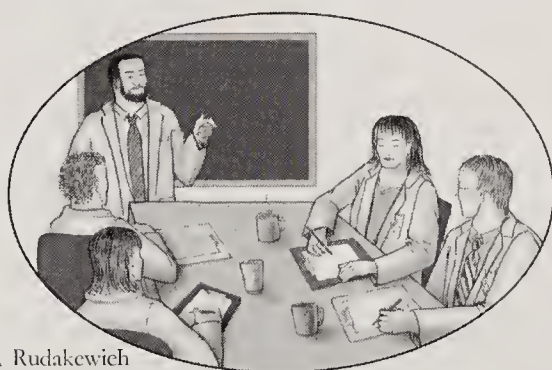
P: Over the next days, the creatinine continued to rise going to 493 mmol/L on post-operative day 15. One day previous, he developed atrial fibrillation. He remained non-oliguric.

Dr. S: Non-oliguric renal failure has a better prognosis than oliguric renal failure. Still, his creatinine clearance must be very low and dialysis may soon be indicated. Does he have any indication for dialysis such as uremic manifestations like encephalopathy or pericarditis, unresponsive fluid overload, hyperkalemia or severe acidosis?

If this is simply ATN, I am surprised that things are still deteriorating so long after removal of the precipitant(s). I must revisit the issue of cloxacillin-induced acute interstitial nephritis and would also reconsider the possibility of immune complex glomerulonephritis stemming from the endocarditis. A renal biopsy would be helpful at this time. However, two important points need emphasis. First, his anticoagulation would need to be stopped for the biopsy. Yet, his "huge left atrium," atrial fibrillation and mechanical heart valve place him at extreme risk for systemic embolization in the absence of anticoagulation. I would, therefore, be loath to stop his anticoagulants for the purpose of biopsy. Second, even if the biopsy reveals a treatable etiology for his renal dysfunction, it would almost certainly be an etiology which is treated with glucocorticoids. Therefore, one could make a case for giving corticosteroids on speculation. This would avoid the risk of reversing his anticoagulation and would treat the two most probable causes of his ongoing renal dysfunction.

I am now treading on very thin ice. As a general principle, one does not use potent medicines in the absence of a clear indication and diagnosis. Nevertheless, I believe a therapeutic trial of steroids is reasonable for the aforementioned reasons. The potential net gain from such a trial outweighs, in my opinion, the potential net harm. The thin ice could be thickened by deciding in advance how long a trial we would use and what criteria would be invoked to determine if he has had a satisfactory response. I would give him steroids.

P: The patient was started on methylprednisilone treatment. Seventy-two hours later, his creatinine began to decline. Four weeks later, on a tapering dose of glucocorticoid, the creatinine was 155 mmol/L. Following discontinuation of the steroids one week later, his creatinine remained stable and has continued to do so to the time of this writing. There has been no evidence of persistent infection in his heart or elsewhere.



Myra Rudakewich

Dr. S: We will never know whether it was the steroids or simply time itself that led to the resolution of his renal failure. That is the most unsatisfying part of so-called "therapeutic trials." Regardless, he is a lucky man.

Table 1
Clinical Pearls

- Bacterial endocarditis can present acutely as well as subacutely
- Endocarditis frequently occurs in the absence of identifiable antecedent risk factors
- Sometimes it is necessary, and acceptable, to make clinical decisions without having all the pertinent facts

Commentary

We thank Dr. Steven Shumak for participating as our expert clinician in this inaugural edition of the *Morning Report* series. His discussion highlights several important principles in the diagnosis and management of a serious, yet treatable, condition. Dr. Shumak illustrates how in practice a high index of suspicion and the anticipation of complications can lead to prompt and life-saving treatment decisions, even before a definitive diagnosis can be reached. This is exemplified in this case by the institution of empiric antibiotics before blood culture results were available, the early surgical intervention before further cardiac complications arose, and the empiric steroid therapy without a diagnostic renal biopsy. The case also reminds us that patients in hospital need to be followed closely with repeated assessments as their conditions may evolve over time. Finally, here is an example where good patient education (which led to the patient's early presentation to the ER and relevant history) proved to be life-saving.

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Obstetrical Rounds

Kelly Grant, BSc. (OT0) and Ali Islam, BSc. (9T9)

A 29 year old G₂P₁ female consented to have a Maternal Serum Screening (MSS) test at 16 weeks of pregnancy. The following results were obtained:

Table 1
Laboratory Results from MSS

		Comment
Alpha-fetoprotein:	166.2 ug/L 3.59 MoM	High
estriol:	3.2 nmol/L 1.10 MoM	Normal
human chorionic gonadotropin:	29.8 kIU/L 1.31 MoM	Normal

What does the elevated alpha-fetoprotein level suggest?

A scan of the fetus spine using ultrasonography was obtained (Figure 1).

What is the abnormality in the spine?

Using the information from the MSS and the ultrasound, what condition does the fetus most likely have?

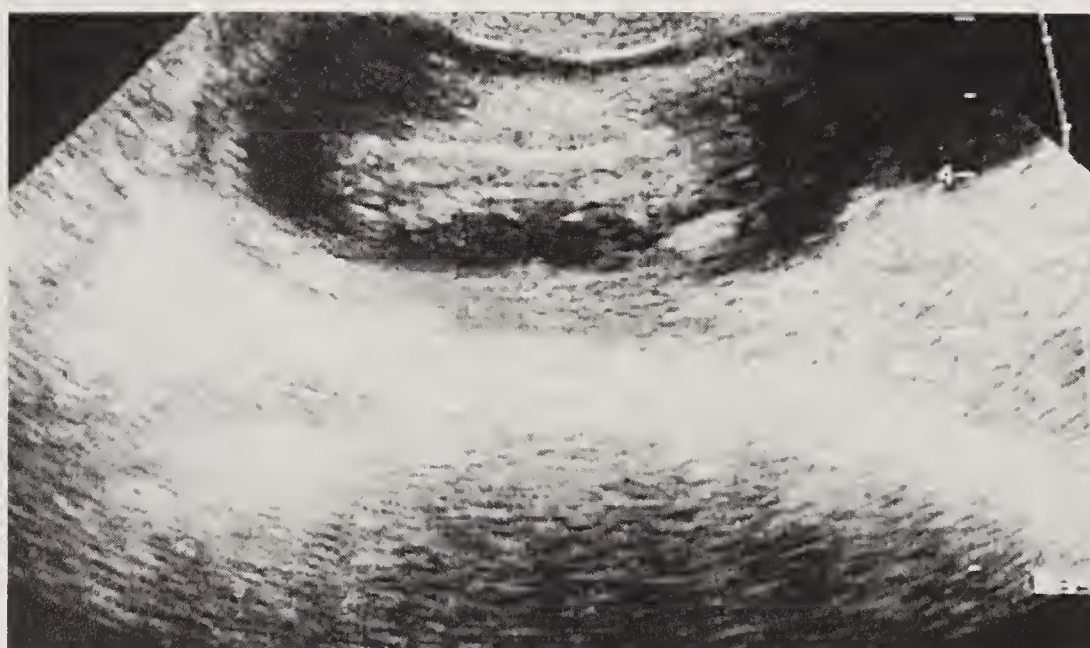


FIGURE 1. *Fetal ultrasound at 18 weeks of pregnancy.*



FIGURE 2. The lateral plain film of this child's spine shows multiple defects in the lumbosacral and sacral vertebra including sacral asymmetry and partial agenesis.

Answers

The MSS is an optional test that is best performed between 16 to 17 weeks of gestational age.¹ The screening test shows who might have a higher or lower chance of having an open neural tube defect, Down syndrome, or other abnormalities. Tests such as an ultrasound and/or amniocentesis can often confirm the diagnosis.

Alpha-fetoprotein (AFP) is a protein almost exclusively synthesized by the fetal liver. Filtration of blood through the fetal kidney results in high concentrations of AFP in the amniotic fluid. The mechanism of transfer of AFP to the maternal circulation is both transplacental and transamniotic. The protein is found in the serum of all pregnant women. It is elevated when the fetus has a neural tube

defect, and is decreased when the fetus has Down syndrome.² Other less common causes for an abnormal AFP level include ventral wall defects (omphalocele, gastroschisis), trisomy 13 or 18, renal agenesis, fetal demise, multiple gestations, and maternal hepatoma.

The MoM (multiples of median) is a ratio of the patient's AFP to the median AFP for a large sample of women at the same gestational period. The neural tube defect screen cut-off is 2.20 MoM. Therefore, the MSS suggests that the fetus may have a neural tube defect. The risk of a neural tube defect, based on this sample alone is 0.003.

The ultrasound taken of the fetal spine is a direct finding of a neural tube defect, since there is a widening and flaring of the spinous processes in the lower spine. Given this ultrasound, the most likely diagnosis of the fetus is spina bifida caused by the open neural tube defect.

Discussion

Spina bifida is a congenital anomaly of the spinal cord that results from a defective closure of the neural tube during the fourth week of fetal development.³ Developmental disorders of the pediatric spine are characterized by incomplete fusion of midline structures. The defects



FIGURE 3. This T1 weighted sagittal MRI shows skin and a large fat pad (lipoma) covering a lumbosacral defect. This is known as a lipomyelomeningocele. Bony anomalies consist of large defects in the spinous processes and laminae. The spinal cord is tethered to fat in the spinal canal and tethering is associated with bowel and bladder dysfunction.



FIGURE 4. Infant born with a myelomeningocele.

can involve the meninges, spinous processes and laminae, muscle, and skin (Figure 2). Spina bifida ranges from clinically significant types to minor anomalies that are clinically unimportant.

In the most minor form, spina bifida occulta, the defect in the vertebral arch, results from the embryonic halves failing to fuse in the median plane. Occulta spinal dysraphism should be suspected if there are midline hemangiomas, hairy patches or subcutaneous patches overlying the spine in the newborn. Although spina bifida occulta usually has no clinical symptoms, children can present with neurological findings related to defects in the spinal cord and spinal roots.⁴

Spina bifida aperta includes spinal dysraphisms in which the skin covering is completely deficient. This includes meningoceles and myelomeningoceles, which are related to hydrocephalus and herniations of the brain into the spinal canal. Spina bifida cystica refers to dysraphic conditions that have a poorly epithelialized membrane, such as lipomyelomeningocele (Figure 3). Recently, the terms spina bifida aperta and cystica have been used interchangeably, which may cause some confusion in the literature.⁵ These abnormalities usually occur in the lumbosacral region, but may appear anywhere along the spinal column.

With meningocele there is a cyst-like sac that protrudes from the defect in the vertebral arch. The spinal cord and spinal roots are in the normal position, but the sac contains meninges and cerebrospinal fluid. There may be associated spinal cord abnormalities that cause urinary and fecal incontinence, urinary tract infections, weakness, or paresthesias in the lower limbs.⁶ A meningomyelocele also contains a cyst-like protrusion from the defect, but includes the spinal cord and/or nerve roots (Figure 4). This condition is often associated with marked neurological deficits below the level of the sac, since nervous tissue is unable to develop normally in the sac.

Risk factors for spina bifida include use of valproic acid, or carbamazepine, and maternal diabetes mellitus. A protective factor is periconceptual folic acid supplementation of 0.4-1.0 mg/day in women who might become pregnant.⁷ Indeed, half of all cases of spina bifida are preventable by folic acid supplementation.⁸

Acknowledgements

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The First 25 Years

In December of 1923 the *University of Toronto Medical Journal (UTMJ)* published its first issue. Over the next seventy-five years, the *UTMJ* has effectively chronicled the ever-changing face of medicine, particularly at the University of Toronto. The *Journal* was founded by medical students and to our knowledge, is the oldest student medical journal in North America. In commemoration of this exciting 75th

year of publication, the current editorial board has established a special section entitled *From the Archives* which will showcase some of the most memorable and insightful research, editorials, and photographs previously published in the *UTMJ*. Each edition of *From the Archives* will encompass a twenty-five year time period, beginning with this issue . . . **the first 25 years: 1923-1948.**

In order to fully appreciate the history of the UTMJ it is important to become familiar with the fundamental principles by which the Journal was originally founded. To facilitate this understanding, we revisit, in its original form, the Editorial from Volume 1, Number 1, dated December of 1923.

VOL. I

DECEMBER, 1923

No. 1

EDITORIAL

WITH this first issue of the UNIVERSITY OF TORONTO MEDICAL JOURNAL we mark an epoch in the history of the undergraduate body of the Faculty of Medicine. We are attempting to do something hitherto untried, as far as we can ascertain, in any medical undergraduate body on this continent, although we have examples of undertakings of a similar nature in some universities in Great Britain. We feel that the JOURNAL will have a definite place and mission in this faculty and with the help of staff and students, we will make it a useful acquisition to the medical student's literary equipment.

The mission of the JOURNAL is two-fold. Firstly—it has been felt that the writing and preparation of papers should be more encouraged among the students. It is one of our ultimate aims to have a journal or writing club—the name is immaterial—organized in each year on a voluntary basis. Particularly good papers would be handed on to the student body through the medium of the JOURNAL. A very successful voluntary writing society has been in operation at the University of Edinburgh for many, many years. Secondly—there are appearing constantly in the current literature, articles and accounts of recent researches which would be of inestimable value to the student. For the most part, the average medical student seldom sees an Association Journal of any kind. We, therefore, plan to reprint for him, from time to time, outstanding material that may appear. We may cite an example. In an early issue we hope to reproduce, with the courtesy of the *British Medical Journal*, an article by Sir Thomas Lewis entitled "Cardiological principles in General Practice". This is a classic and should be in the hands and head of every medical student. Yet, we will venture to say that not two dozen undergraduates have heard of it, let alone read it.

One can visualize the many important departments that may develop in a publication of this nature. New books may be reviewed; notes may be made from current literature; as time goes on a valuable Alumni connexion should be established, and so on. For the first while, we will be dependent on interested members of the staff for a considerable quantity of our material and incidentally we hope that each issue will contain a leading article of universal interest from one of the faculty members who may be doing advanced work along some particular line. Individually, the members of the staff of the Faculty of Medicine are enthusiastic in their support of the project, although as a whole they have no responsibility in the matter whatever.

We urge all, students and professors alike, to give us their wholehearted support in our effort for the still further advancement of this faculty in the medical world.

Founding Fathers

To express our gratitude to our founding fathers a 1923 photograph of the original editorial board is included as we wish to thank them as well as all the previous editors for their ingenuity, creativity and perseverance.



STAFF OF UNIVERSITY OF TORONTO MEDICAL JOURNAL, 1923-24.
TOP ROW—A. H. Walker, H. E. Bicknell, C. A. L. Campbell, K. G. Gray.
BOTTOM ROW—N. A. McCormick, E. P. Scarlett, D. M. Meekison, R. S. Stone.
INSERT—R. P. Mackay.

Part of Tradition

Even though many things have changed since 1923, the 1997 edition of the *UTMJ* still beholds the same ideals as those of the original journal; namely, to convey information of academic and practical interest to the medical students as prepared by fellow medical students. One only needs to look at the long and distinguished list of publications by students over the years to know that these ideals have been preserved. In addition to the ideology, many published works from the journal have sustained their relevance and application throughout the years. This includes the following pearl entitled “Myopia,” which first appeared in November of 1925, and clearly demonstrates that works of true value will stand the test of time.

“MYOPIA”

THERE are few undergraduates who do not at some point in their course in the earlier years become disheartened by the seemingly useless detail of innumerable subjects. Many do even seriously question the judgment of those who design the medical curriculum. Yet there seems just one thing to do—accept it all and “muddle on”.

The early years are the “stoney age” and one is dealing with the elements of medical science. The first three years in turn seem only to add so much more of that which appears unrelated to the cure of disease. This is the point where, if it were possible, a glimpse at the clinical side of medicine would rekindle enthusiasm and help to overcome the monotony.

For those who suffer from this distortion of vision we promise it is transient, and suggest that they recall their knowledge of the spectrum and remember that the colour elements, many of them vague are all necessary before the pure band of light is possible. This philosophical prescription if thoughtfully applied may establish a new field of vision and perchance may forestall a crisis.

Sugar Daddies

Although the following biographies were not featured in the *UTMJ*, we would be remiss in excluding the co-founders of insulin, and the pride of the University of Toronto.



Sir Frederick Grant Banting (1891-1941), co-discoverer of insulin. He first entered the University of Toronto to study for the ministry, but transferred to medicine, and graduated in the accelerated course in 1916, a classmate of Norman Bethune. Dr. Banting served in the Canadian army's medical corps and received the military cross. Following the war, he received a minor appointment in London's medical school. It was his reading in the library there that led him to the idea of ligating the pancreatic duct, to permit the extraction of insulin. He joined the staff of the University of Toronto in 1921. Later that year with Charles Best and J.J.R. MacLeod (head of the Department of Physiology), he was the first to obtain insulin in a form consistently effective for the treatment of diabetes mellitus. In 1923, he received the Nobel Prize, and was knighted in 1934. He died in a plane crash while on a war mission in 1941. His wife, Henrietta Ball Banting, subsequently graduated from the Faculty and specialized in cancer research.



Charles Herbert Best (1899-1978), co-discoverer of insulin. He was studying physiology and biochemistry at the University of Toronto as a preliminary to medicine when he assisted Banting in the discovery of insulin. Entering medicine as the University's “most famous undergraduate,” he graduated in 1925, and in 1929 succeeded Dr. MacLeod as head of the physiology department. Serving with the navy during World War II, he was largely occupied in research into the prevention of seasickness. Following the War, he was instrumental in establishing the C.H. Best Research Institute. He shared, at Banting's insistence, Banting's half of the Nobel Prize in 1923. Professor MacLeod received the other half.

A Doctor and a Gentleman

In addition to the obvious scientific value of the *UTMJ*, it has on occasion served to provide invaluable social commentary on the state of medicine and medical students. The following editorial entitled "Personality in Medicine" appeared in the January 1938 issue. Not only does it provide entertainment

for readers today, but it addresses issues that are still pertinent to the present day medical student. Although this editorial certainly has a paternalistic flavour, the essence of the message is relevant to both men and women.

Editorial

PERSONALITY IN MEDICINE.

Everyone recognizes that Personality is important in medicine. And yet we are convinced that in medical education not enough stress is placed upon it. Too much emphasis is laid upon the attainment of an extensive knowledge of cold facts and too little attention is paid to the development of a pleasing Personality. Of course "Personality Training" is not something that can be taught, except by example. It is something which each must develop within himself. We feel that we will be performing a useful service if we remind medical students of the importance of cultivating Personality and indicate some of the ways in which this may be accomplished.

To begin with, we must attempt to define Personality. Naturally that is difficult to do. Perhaps we can indicate our conception of it if we say that Personality is the summation of those factors about an individual which make him attractive to other individuals. To make it clearer, think if you can, of someone whom you are always glad to meet and whom having met, never fails to make you feel that life is a little better than it seemed before. That individual has Personality.

Surely the value, or rather the necessity, of Personality in medical practice is obvious. To begin with it will help you to get through your undergraduate training. In the earlier years it will bring you close friendships with your fellow-students. Making friends is the first lesson in Personality Training and you will rate 100 per cent. in Personality only when you have learned to act in such a way that every acquaintance calls you friend. In the clinical years you will find an ounce of Personality far more valuable than a pound of knowledge. It will win for you the admiration of your clinicians, the coöperation of the nurses (even Supervisors!) and above all, the confidence of the unfortunate patients who must submit to being quizzed and poked and pummelled and squeezed to no obvious advantage. It is easy to "get along" with patients if you treat them kindly and gently. Remember that they are human just as you are. Show a real concern in their being ill and lend a patient and sympathetic ear to their story of troubles both physical and mental. Be cheerful and tactful and act as though you credited them

with at least average intelligence. If you do all these things naturally, as an expression of your Personality, then you will find your patients smiling instead of hiding under the covers as they see you coming down the ward.

And when you graduate, how necessary is Personality! Ask yourself, of what value will be all your hard-won knowledge, if prospective patients on contemplating you are repelled rather than attracted to your office door. And if they do come and you treat only their bodies and not their souls, how great will be your success? There never was a disease cured by the administration of drugs or by surgical operation alone. More than that is necessary. The doctor must inspire confidence in his patients so that they will believe in the efficiency of his remedies. He must be the trusted friend on whom they can rest the burdens of their troubled spirits. After all, nine-tenths of patients need psychotherapy more than they need medicine, and what is psychotherapy but kindness and sympathy and common-sense advice? And to make it effective the doctor must exemplify through his own Personality the worth-whileness of a better life.

With these ends in view it is our contention that medical students should constantly strive to develop within themselves those attributes which will make their Personalities attractive. Some of these,—kindness, gentleness, sympathy, patience, cheerfulness, tact, and trustworthiness,—have been referred to already. They and others are inseparably associated with the concept of a "Gentleman." Some discerning mind has defined a Gentleman as "one who never consciously hurts the feelings of another person." Strive to live up to that definition and you will be a better doctor than you ever thought your ability deserved.

Another aspect of Personality that we would like to stress is a good appearance. For that, expensive clothes and beauty of face or figure are useful accessories, but not essential. Far more important are cleanliness and neatness. Shoes shined, hair parted, trousers pressed, and hands spotless,—what a difference these can make in any man! Remember, first impressions count, and they are usually visual impressions.

Self-confidence is important in Personality. Do you but believe in your own ability and those who come to you for aid will sense that you can help them. Confidence comes with knowledge. But there is another factor, and

that is the experience of working out problems for yourself. Do not be too anxious to copy someone else's work. Struggle through it yourself and you will be rewarded by the conviction that you can rely on your own ability.

The art of conversation is a valuable asset to any man. Dale Carnegie gives away the secret in his book, "How to Win Friends and Influence People."

Find out what the other fellow is interested in, ask a few leading questions, and then let him do the talking. It is a good theory and it works. Of course there are other methods of improving your conversational ability. Have a few interests outside the narrow field of medicine. Do not confine your reading to text-books. Browse through the newspapers once a day and enjoy a good book occasionally. Be able to discuss intelligently the topics of the day. Incidentally we would like to make a plea at this time for the more widespread use of the "King's English." It is extremely gratifying to listen to someone who observes at least the elementary rules of grammar and who speaks clearly so that listening to him is not a constant strain upon the auditory apparatus. It is unfortunate that many medical students tend to be careless in this regard.

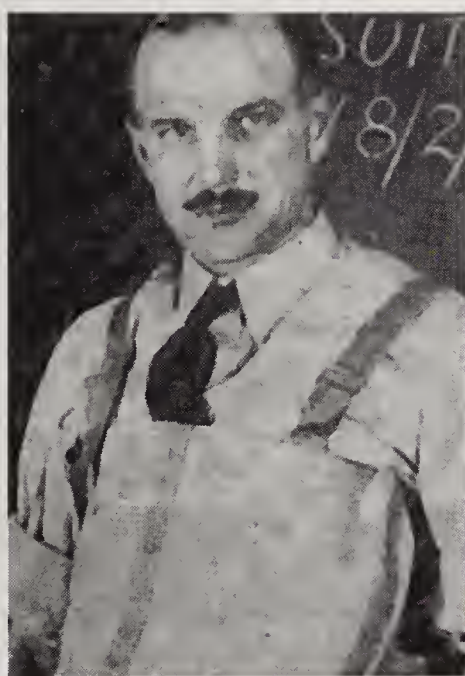
Finally may we advocate a sense of humour? We are not referring to the wit which makes a play on every spoken word and supplies a hackneyed epigram for every occasion. Rather do we mean the ability to be happy about life in general, take reverses with a smile, and see the funny side of other people's humour. It really is a saving grace.

Of course there are many other aspects of Personality that we have not mentioned. But we are well content if we have succeeded in arousing even a little conscious interest in this important aspect of medical education.

R.A.M.

War Effort

A retrospective analysis of this time period would not be complete without a tribute to the faculty, staff, students, and families of the University of Toronto, who honourably served their country in World War II. The war had ramifications felt across the country and throughout all aspects of university life including the *UTMJ*. Much of the research, editorials, and advertisements presented during the war were aimed at the war effort. As the advertisement on this page depicts, the race was on to not only improve all aspects of life for our soldiers, but to also improve the productivity of the individuals involved in the war effort back home in Canada. Although the war-time contributions made by the University of Toronto family are tremendous, the remarkable discovery of the anti-blackout suit by Wilbur Rounding Franks was instrumental in assisting the Allied effort. Thus, a brief biography of this man and his outstanding research follows.



Wilbur Rounding Franks (1901-1986), inventor of the anti-blackout flying suit. He graduated from the University of Toronto's Faculty of Medicine in 1928. He was renowned as a cancer researcher at the Banting Institute and returned to this field after his World War II experiments. In 1942, Dr. Franks solved a problem that had baffled the Allies' best scientists in a project that was one of the top secrets of the war. In his cancer research, Dr. Franks found that glass tubes kept shattering in tests on carcinogens using a high-speed centrifuge. He started experimenting with small tubes in larger ones. Not a single one broke. Applying this principle to his aviation experiments, he created the "G" suit or "anti-blackout" suit. Credited with saving thousands of Allied

fighter pilots during World War II, his invention is worn by every air force pilot in the world, as well as astronauts and cosmonauts. He also designed the world's first centrifuge — a gondola at the end of a rapidly spinning boom and it is now used in training astronauts.

This advertisement appeared in 1942, Vol. 20, No. 2.



● Absenteeism due to illness is retarding our war effort. Study of the underlying causes reveals that, in many cases, the diets of employees are deficient in certain vital food factors. An extensive effort is now being made to improve the national diet but such a programme of public education takes time. Until the importance of proper diet is more generally understood, some supplementary means of providing essential vitamins and minerals should be employed. A daily dose of "Alphamin" can do much to improve the health of Canadian workers and so help to maintain war production at its highest level.



BUTYN

A new local anaesthetic with important advantages over cocaine.

Whether for eye work or for operations of the nose and throat, urologic or minor surgery in general, Butyn is superior to cocaine in a number of respects. Less is required; it acts more rapidly; the anaesthesia induced by it lasts longer.

Phone or write for our booklet No. C326 or our catalogue.

THE ABBOTT LABORATORIES

221 WEST RICHMOND STREET - - - - TORONTO, ONT.

*Although not related to the war effort, this advertisement was regularly found in the *UTMJ* during the same period, appearing first in 1924 Volume 3, Number 1. Apparently this stuff was better than cocaine!*

Infant Elixir

Few of us can admit to growing up without some interaction with Pablum. Whether it was dribbling down our own chin, or those of a friend or relative, the invention of Pablum baby-food at the University of Toronto has had a global impact on post-natal care. This page showcases one of the original *UTMJ*'s Pablum advertisements, along with a brief look at the life and times of the gentlemen contributing to its creation.



Alan Brown (1887-1960), said to be the greatest Canadian paediatrician of his time. He graduated from the University in 1909. Following post-graduate work in the U.S. and Europe, he returned to Canada with the best credentials of any paediatrician then in the country. In 1919, he became Physician-in-Chief at the Hospital for Sick Children, and under him it became one of the finest paediatric hospitals in the world. As an administrator he was a blunt, demanding disciplinarian, but while caring for children his true humanitarianism was apparent. A pioneer in the field of infant feeding, his strict policies greatly reduced the problem of cross infection.



Theodore George Harwood Drake (1891-1959), co-inventor of the infant food Pablum. He graduated from the University in 1914. In 1926, he visited the Finsen Institute, Copenhagen in order to get further information on ultraviolet-light therapy. This was an invaluable experience for his future work in the measurement of sunshine and the development of Pablum. From 1949-54, he was Director of Research Laboratories at the Hospital for Sick Children. Dr. Drake was an ardent collector of antique objects relating to the care and welfare of infants and children. During his 35 years of collecting, he assembled over 3,000 specimens dating from Egyptian, Greek and Roman times to the 19th century. Following his death, Mrs. Drake donated the T.G.H. Drake collection to the Academy of Medicine, Toronto.



Frederick FitzGerald Tisdall (1893-1949), co-inventor of Pablum. He graduated from the University of Toronto in 1916, and early in his career took a special interest in the health care of children. He originated a health scheme throughout Toronto schools to study the dietary habits of children. In 1927, his experiments with natural rays of the sun for promotion of acidity in the intestinal tract won him fame throughout his profession. In addition to these research projects, Dr. Tisdall devoted much time to the health of the Indians in the Canadian north. In 1930, Drs. Tisdall, Drake and Brown published an article in the *American Journal of Diseases in Children* entitled "A New Cereal Mixture Containing Vitamins and Mineral Elements". This modest sounding title was actually the first official announcement of Pablum. ■

Ladies Only

The fourth edition of Volume 11 in 1934 was exclusively written by women. Indeed the history of women in medicine has undergone a long and tortuous course. The editors of that 1934 issue noted it was "not a foolish attempt to segregate the sexes even in their writings, but just an experiment undertaken in the hope of eliciting a little friendly competition." In the same issue, there appeared an article describing the official plans of the new building for

Women's College Hospital. With the ever-changing face of medicine, and the near certainty that Women's College Hospital will undergo some form of restructuring in the future, this hope-filled 1934 article is presented in tribute to the century of contribution Women's College Hospital has made to medicine and to the *UTMJ*.

THE WOMEN'S COLLEGE HOSPITAL

HARRIET MEIKLEJOHN, R.N.
Superintendent, Women's College Hospital.

The above is the end of the proposed New Women's College Hospital, so long anticipated by those interested, and which is about to be erected in the very near future. This Hospital will be constructed on the square now owned by the Hospital, bounded by Grenville Street, Surrey Place and Grosvenor Street, with a lane on the east side.

The Women's College Hospital is a general hospital for women staffed by women physicians and surgeons and the only one of its kind in the Dominion of Canada. It will comprise the Services of Surgery, Gynaecology and Urology, Medicine, Obstetrics, Oto-Laryngology, and Out-Patient Department. The new building has been long needed. The Out-Patient Department had some 20,000 visits in the past year. The in-patients in the present 60-bed hospital numbered over 2,000 with a steady waiting list of over 100 patients, and we have usually in the neighborhood of 600 births a year.

This hospital is a long and interesting history of the growth and development of Woman's endeavour for Woman, and it shows an even, steady growth over its thirty years of existence. In our new quarters we will be able to accomplish a greatly augmented piece of work and care for the patients who would like to come to us and whom we have been unable to accommodate.



In the central east to west portion of the above picture which is now to be constructed, will be a complete hospital unit. In years to come as need arises and accommodation requirements demand, the wings of the hospital can be added. There will be accommodation for private, semi-private, public and city order patients in all of the above services. The public wards will accommodate from four to six beds, and provision has been made for many small single rooms to rent at moderate prices as well as for a few more elaborate rooms for those who wish for better

accommodation. About 150 beds and 60 infant cots will be provided in this first unit and in the final analysis the hospital should comprise some 300 adult beds.

As well as the above, the new building will house operating rooms, maternity case rooms, with all necessary accessories sufficient to meet the needs of the number of beds provided. The laboratory will be provided with space for pathology, bacteriology, blood chemistry and museum. There will be a modern X-ray department with provision for cystoscopy and fracture work, an admitting department and detention ward. The building will also accommodate kitchens and dining rooms with all service requirements, an office and waiting rooms and all the many accessories of a general hospital.

We believe that our hospital will be easy of management, and control, and economical in that we are building up in the air rather than over a large ground area. Patients' accommodation will begin on the third floor and as the wings are added, we should have very excellent roof exposure, facing full south with a beautiful view over the down-town section of Toronto and out over the lake.

We are greatly looking forward to the day when we will be able to turn our first sod.

In Closing

To close out this first segment of *From the Archives*, we focus on an editorial gem which appeared in March 1939 regarding the rapidly changing position of the physician in society. The editorial text is lengthy and for brevity sake it appears only as an excerpt. Nevertheless, it is clear that the trials, tribulations, and concerns of practising physicians transcend the years. More than fifty years ago, the topics at the forefront of medicine included the socialization of medicine, the employment of physicians as salaried government employees, and the lack of physicians in northern rural areas. The final paragraph is especially poignant and is presented as it appeared 58 years ago.

All these problems are of real interest to the medical profession. The individual physician is not in favour of any radical change. He does not want to become a government employee and lose much of his independence. But whether or not socialized medicine will evolve depends largely upon the influences acting on the medical profession. Medical organization is changing with the social conditions. The next fifty years will likely see great advances in the social organization of medicine.

Imaging Atlas of Human Anatomy

Sam Minor, BSc. (OTO)

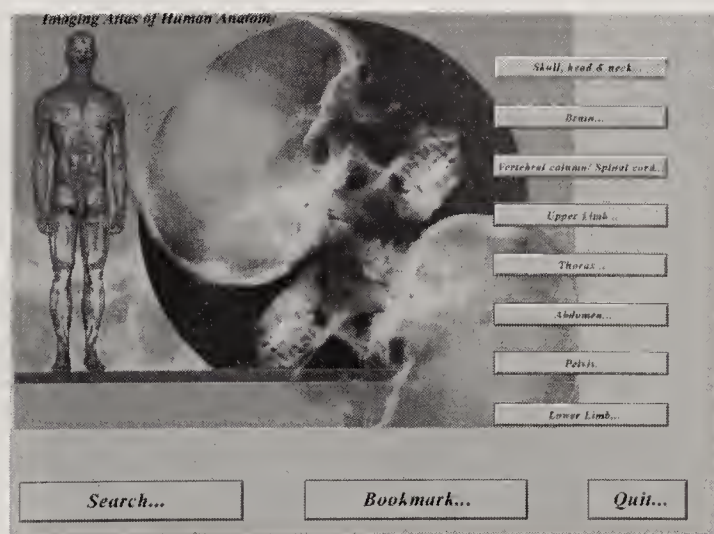
The Imaging Atlas of Human Anatomy by Mosby Multimedia is a great radiology atlas that allows rapid retrieval of images on any part of the body. The program is extremely easy to use, interactive and has stellar graphics. It is navigated by a "point-and-click" interface. Images can be accessed by either anatomical region (e.g. thorax, abdomen, etc.) or by imaging modality, or both (e.g. only MRIs for each region). The program also permits keyword searches where you can type in what you are looking for, for example "stomach," and it will list all the images in the atlas representing that body part or region.

Individual images can be viewed in any of three formats. The first is similar to the figures found in most anatomy atlases, in which the anatomical structures on an image (photograph, x-ray, MRI, CT etc.) are labeled using arrows and text. The second format has dots placed on the images and a list of labels on the side. When a dot is "clicked," the appropriate term for the anatomical structure appears. This feature is useful as a test of anatomical knowledge. Finally, the program can generate a series of self-quizzes. It will challenge the user to find an

anatomical structure by using the mouse to point to the correct location.

The atlas also offers a complete set of MRI and CT pictures of the brain that are especially valuable for anyone studying neuroanatomy. In addition to neuroimaging, the entire body is represented by x-rays, CT and MRI. More frivolous, but interesting, features include quick time videos showing ultrasound and MRI examinations. It is a fantastic review of anatomy for students in both undergraduate and professional programs.

The only drawback to this CD-ROM lies in its scope. Although it is not intended to be an index of medical diseases, this atlas might benefit from useful examples of common or informative pathologies and disease processes that cannot be included in text atlases due to lack of space. For the truly determined student, comparable images and examples can be found (without the cost of purchasing a CD-ROM) by searching the Internet. However, this package does a very good job of collecting, organizing and displaying human anatomy.



C : \ Quick \ Reference \ Review

Imaging Atlas of Human Anatomy

List Price: \$69.95

Mosby Multimedia, St. Louis MO; 800-325-4177

<http://www.mosby.com>

System Requirements:

IBM or compatible PC, 486 DX, 8 MB RAM, 640 x 480 VGA 256-colour or more display, CD-ROM drive, Sound Card, Microsoft Windows 3.0 or more

Target Population: Anatomy students in any undergraduate or professional school course.

Rating (out of 5):★★★★

EndNote 2 Plus (with EndLink 2)

Brian Buck, MSc., (OT0)

Formatting references for a manuscript or report that contains more than a handful of references can be a tedious and time consuming task. EndNote is designed to make reference management a simple process that can be completed in a matter of minutes rather than hours. On the surface, EndNote is a database program that allows you to maintain a library of up to 32,000 references. However, the real power of EndNote is the program's ability to integrate itself into your word processing software and to automatically format citations and build a bibliography that conforms to over 200 journal styles.

Entering references into an EndNote reference library can be accomplished by two methods. The references can be entered manually by typing the information into a window that contains separate fields for the different parts of a reference (e.g. authors, journal name, title, abstract etc.). Alternatively, and more efficiently, references can be directly imported from on-line databases such as MedLine. Using this approach, it takes only a couple of minutes to download a MedLine search to an e-mail account and then import the search results into an EndNote library. The imported references can include the abstracts and keywords and have the added benefit of being free from typographical errors.

Once references are entered into a reference library, EndNote provides a number of tools for managing the database. The references can be sorted and searched by any of the fields, including the abstract and keywords. The search engine also supports complex searches that can include Boolean operators. These search features make EndNote an excellent program for organizing and cataloguing a growing pile of medical literature, in a format that allows for the quick retrieval of relevant information.

With EndNote, incorporating references into a manuscript is a straightforward process. EndNote comes with an Add-in that is compatible with current versions of both Microsoft Word and WordPerfect (Windows and MAC versions available). The Add-

in allows you to access EndNote references and formatting commands directly from the Tools menu of your wordprocessor. To insert references into a document, you simply select the reference(s) that you want to cite and then choose Insert Citation from the Add-in menu in your wordprocessor. This will insert a temporary citation directly into your document. When you are ready to generate the bibliography and formatted citations, you select Format Bibliography from the wordprocessor menu. EndNote then replaces the temporary citations with formatted citations and creates a bibliography according to the selected reference style. The style library includes most major biomedical journal formats and has the additional capability of defining new styles. EndNote also makes it easy to reformat documents multiple times, which is useful in cases where a manuscript has to be resubmitted to a new journal.

Overall, EndNote is a powerful package that eliminates the hassle of dealing with references and allows you to focus on your writing. The only weakness lies in the "look-and-feel" of the program. The user interface is not as sophisticated as other recent Windows 95 applications. For example, EndLink commands are not accessible through a toolbar or the right mouse-button. With this minor complaint aside, the program's features are easy to use, well documented and can be mastered in a couple of hours. Although many software packages claim to help you become more productive and efficient, EndNote is one of the rare applications that truly hits the mark.

C : \ Quick \ Reference \ Review EndNote 2 Plus

List Price: \$295 (Academic Version)
Niles & Associates, Inc. Berkeley, CA; 800-554-3049
<http://www.niles.com>

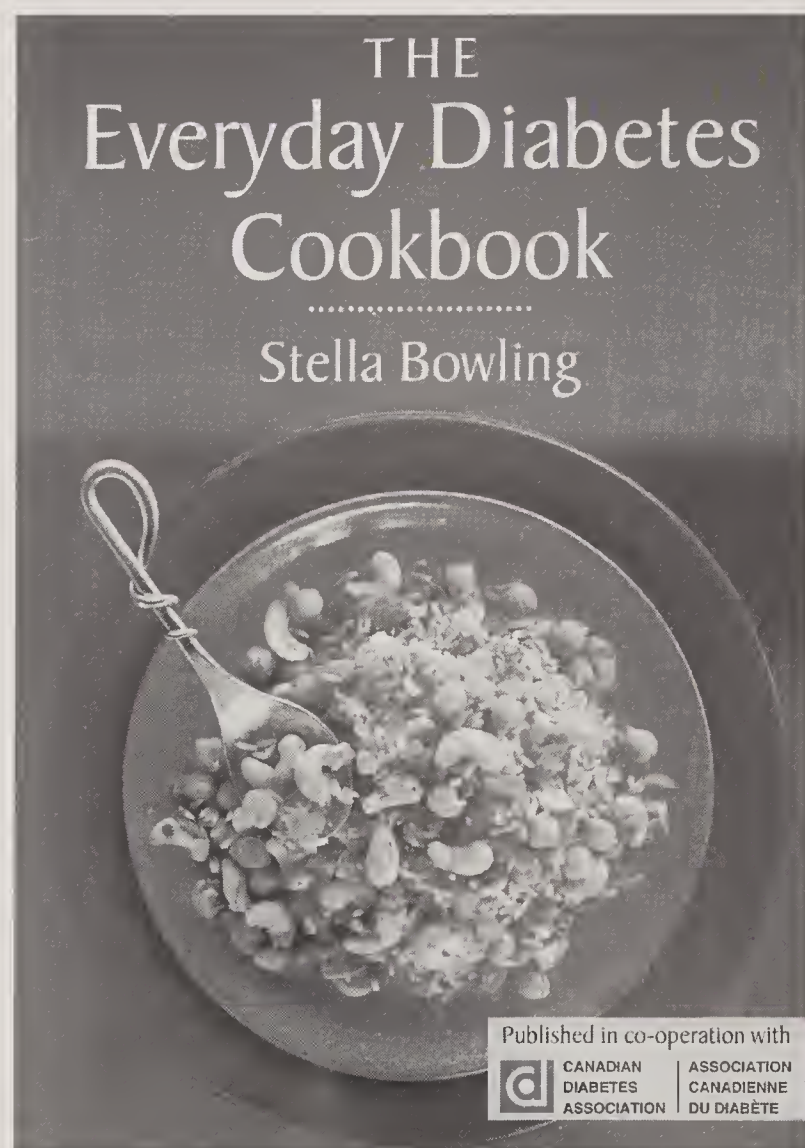
System Requirements:
PC with 386DX/25 MHz or higher with Windows 3.1 or later.
Hard drive with 4MB RAM. (MAC version also available)
Rating (out of 5):★★★★

The Everyday Diabetes Cookbook

Reviewed By Marc Kerba, BSc. (OT0)

Written by: Stella Bowling
Canadian Diabetes Association, Key Porter Books, 1995
British Diabetes Association
Pages 176.

Overall Rating:	Good to Excellent
Strengths:	Simple recipes, details on nutritional content, wide variety of recipes
Weaknesses:	Doesn't discuss diabetes and reasons for strict diet
Audience:	General public, mostly diabetics



Eating may be one of life's greatest pleasures, but the enjoyment of creative, culinary wizardry is also very rewarding. *The Everyday Diabetes Cookbook* was cooked up in collaboration with the Canadian Diabetes Association. However, it should not be regarded as literature solely for the gastronomic delight of English-speaking diabetics. With more than 140 original

and balanced meals supplemented by a nutritional analysis of calories per serving, fat, protein, and carbohydrate content, this cookbook most definitely appeals to the adherents of a healthy lifestyle. Also of help are the extra bits of information provided in the margins about variations on meals and ingredient substitution.

As a devout believer in easy, fun and tasty meals, this book is the equivalent of "haute cuisine meets Betty Crocker." For example, an easy-to-make beef, pepper, and baby corn stir-fry is offered on page 65. Besides its simplicity in preparation, it was delicious. At less than 400 calories per meal, the only excess must reside in the temptation to eat your friend's dinner. There are 139 other more involved recipes in total and the beauty resides in their simplicity. Take the strawberry milkshake on page 155. It is awesome and at 102 calories a glass, it is recommended to make it by the pitcher. This cookbook is designed with the average chef in mind. However, culinary skill does vary with the chef.

This cookbook is very useful to diabetics because it follows the dietary symbols and equivalencies used in a diabetic diet. As such, this book helps eliminate any possible confusion arising from food category choices. This is how *The Everyday Diabetes Cookbook* differs from its competitors. Consequently, adherence to a dietary regimen may be improved. Furthermore, lacking is any sort of basic information about diabetes and its variations and complications. These factors should be stressed because a well-balanced and well-controlled diet significantly reduces health complications. Knowing the dietary regulations in controlling diabetes is important information for diabetics and/or those caring for them.

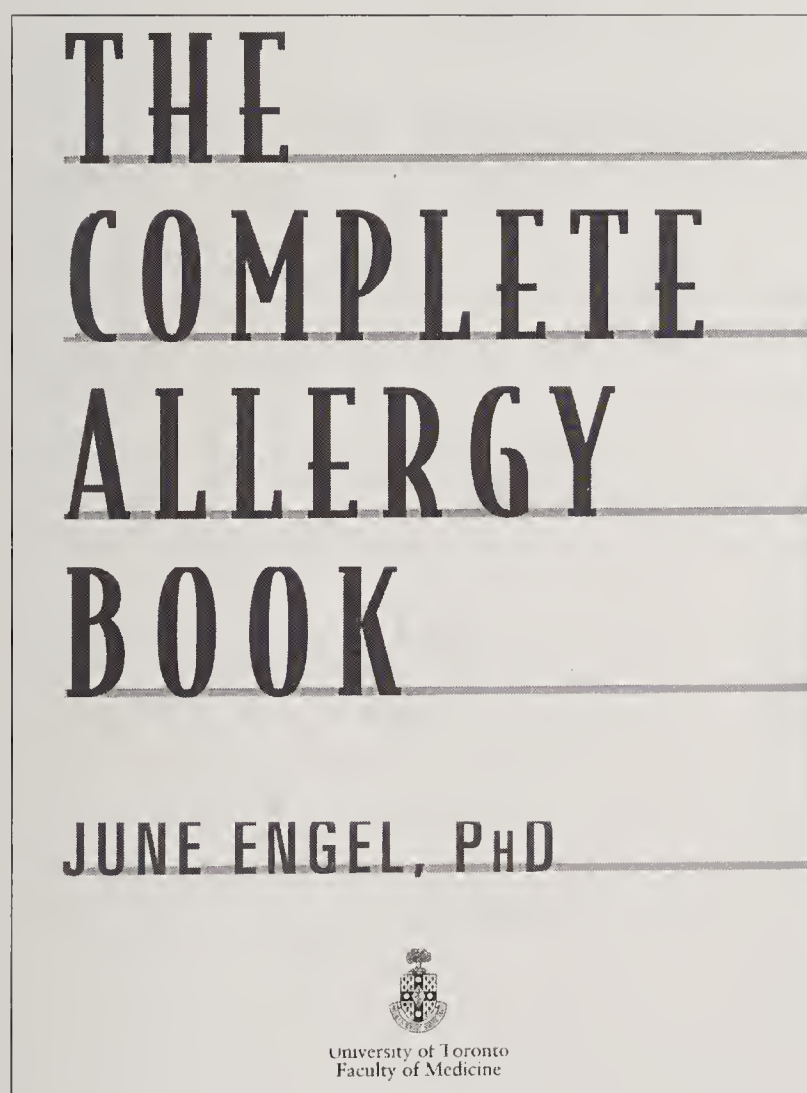
In summary, the author should be commended on her balanced attempt at presenting delicious alternatives to your standard breakfast, lunch, and dinner. Perhaps for a second edition, a more extensive cookbook should be offered.

The Complete Allergy Book

Reviewed By Craig Railton, Ph.D (OT0)

Written by: June Engel, Ph.D
Key Porter Books, Ltd., 1997
Pages 318.

Overall Rating: Excellent
Strengths: Clear, plain English, good practical skills
Weaknesses: A few minor technical wording mistakes
Audience: Practitioners, students, and general public



This book is a very easy read. The English is clear, simple, and easy to understand. I enjoyed *The Complete Allergy Book* because it is a refreshing contrast to many medical textbooks.

It was not clear, based on the introduction, for whom this book was written. I suspect the audience is physicians and medical students. The author wrote the book at a level which most well-educated peo-

ple should be able to understand. She does not use long words excessively, and when she does, the meaning of each word is explained. There are also many inserts in the book summarizing key points. She includes many tables of medications, which are quite comprehensive and useful to students. I am not certain if everyone who graduated from high school would understand the entire book, but I believe that most people should walk away with some helpful suggestions.

This book covers the topic of allergies, including subtypes, diagnosis, and management. It also deals with asthma and anaphylaxis. The advice given is sound and the author often emphasizes the importance of seeking expert opinions when people believe they have allergies.

Certain sections of this book struck my funny bone. I am sure Dr. Engel never intended for her suggestion of washing one's cat to prevent allergy suffering to be funny. However, I found myself remembering a childhood experience of trying to wash a cat. I can only say I was lucky to have not caught cat scratch fever and do not recommend that anyone repeat this activity. The point of my story is that although most suggestions in the book are practical, there are a few which would be difficult to put into practice.

At one point in this book, a technical term is not defined correctly. Dr. Engel defines the word hydrophobic to mean "water-loving," when the word really means "water-fearing." This is a minor mistake which should have been caught by an editor.

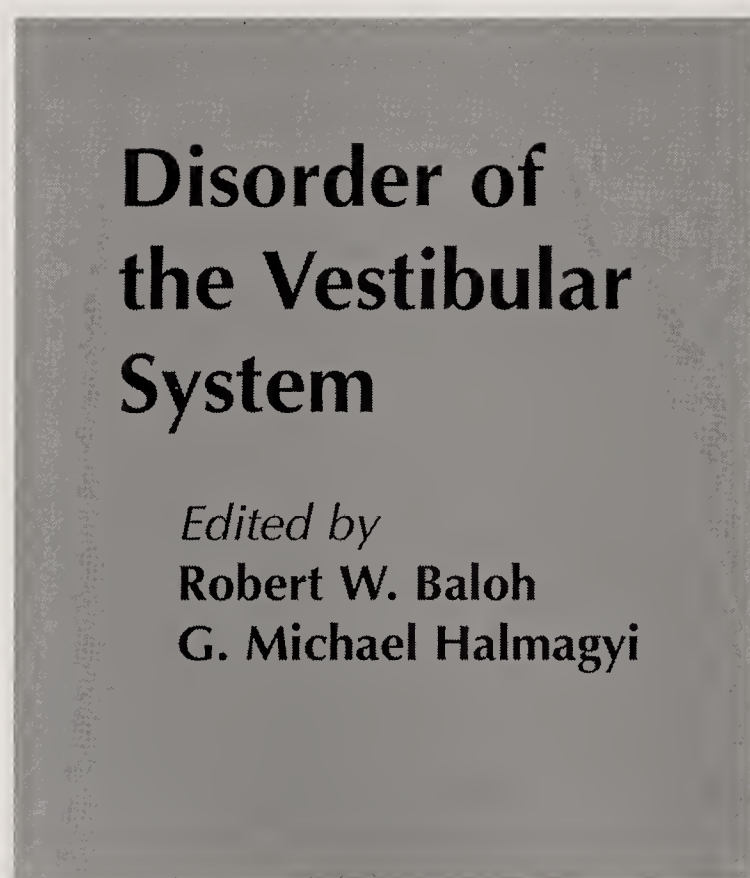
Since approximately 10-20% of the populace suffers either from an allergy or asthma, I think that *The Complete Allergy Book* is an excellent resource for physicians as a review, or for students as a starting point for this subject. This book contains a great deal of practical advice and I would recommend this book to all who are interested, but advise that any physicians who recommend the book to their patients should be ready to answer questions regarding technical explanations.

Disorder of the Vestibular System

Reviewed By Michael J. Angel, Ph.D (OT0)

Written by: Robert W. Baloh and G. Michael Halmagy
Oxford University Press, 1996
Pages 600.

Overall Rating: Superb
Weaknesses: Expensive
Audience: Neurologists, otolaryngologists



Baloh and Halmagy have assembled an astonishingly in-depth and up-to-date review of the structure, function and pathophysiology of the vestibular system. This 600 page tome is made up of 46 chapters organized into four main sections: I) Basic Vestibular Mechanisms, II) Clinical Evaluation, III) Common Vestibular Disorders and Diseases, and IV) Treatment of Vertigo. Each chapter is a manageable 10 to 20 pages and is written by the leaders in the field. A great deal of Section I is devoted to experimental evidence for mechanisms of the vestibulo-

ocular reflex (VOR) and its adaptive plasticity, and the coordination of head/body and eye movements. This section is rife with theoretical models and will appeal to hardcore graduate students studying the vestibular or oculomotor systems, or for neurophysiologists with similar interests. Much of Section I requires an advanced understanding of vestibular system experimentation and is thus beyond the scope of most medical students and physicians who do not have a particular interest in this field. Section II provides a superb overview of the bedside assessment of vertigo and dizziness. This section is easier to read than Section I, and the clinical framework and practicality of the information is presented clearly. Included in this section is an excellent summary and rationale of a history-taking for the dizzy patient with a step-by-step analysis of the exercise. The remainder of Section II is a detailed review of the laboratory evaluation of vestibular structure and function. These include: electrooculography; MR and CT imaging of the vestibular apparatus (both normal and diseased); otolith and auditory testing and posturography and vestibular evoked potentials. Aside from the chapters on the history of the vertiginous patient and the differential diagnosis of vertigo, the bulk of this section is beyond the needs of the medical student. Section III provides an extensively detailed description of vestibular diseases and disorders and is followed by a detailed approach to treatment of vertigo summarizing the strategies and rationale for pharmacological, surgical and rehabilitation methods in Section IV. In most of the chapters, summary tables are provided for differential diagnoses, and other need-to-know information. By distilling large amounts of information in easy to use tables, this book was user friendly and useful for quick reference.

Disorder of the Vestibular System provides a rare combination of both extensive experimental and clinical reviews of the physiology and pathophysiology of the vestibular system. With a reference list of over 2300 articles this is an extraordinary reference text. The writing styles and organization of each chapter vary considerably, but this is not surprising since the book covers a broad spectrum of topics and is the combined efforts of 54 authors. There is considerable repetition of descriptions of anatomy and physiology of the vestibular system across the four sections, however this works well as it allows each chapter to stand

on its own. Baloh and Halmagyi state that the text is aimed at “those in the field of neurology, otolaryngology, head and neck surgery” or students entering one of these fields. At a cost of about a third of a month’s rent in Toronto (\$193.00) the authors will alienate all but the hyper-keen student wastrels. However, if you have the money, and see yourself as a budding otolaryngologist, go for it. This text will provide you with months of enriching insights into the workings of the inner ear, its role in coordination and motor control, and diagnosis and treatments of its associated diseases.



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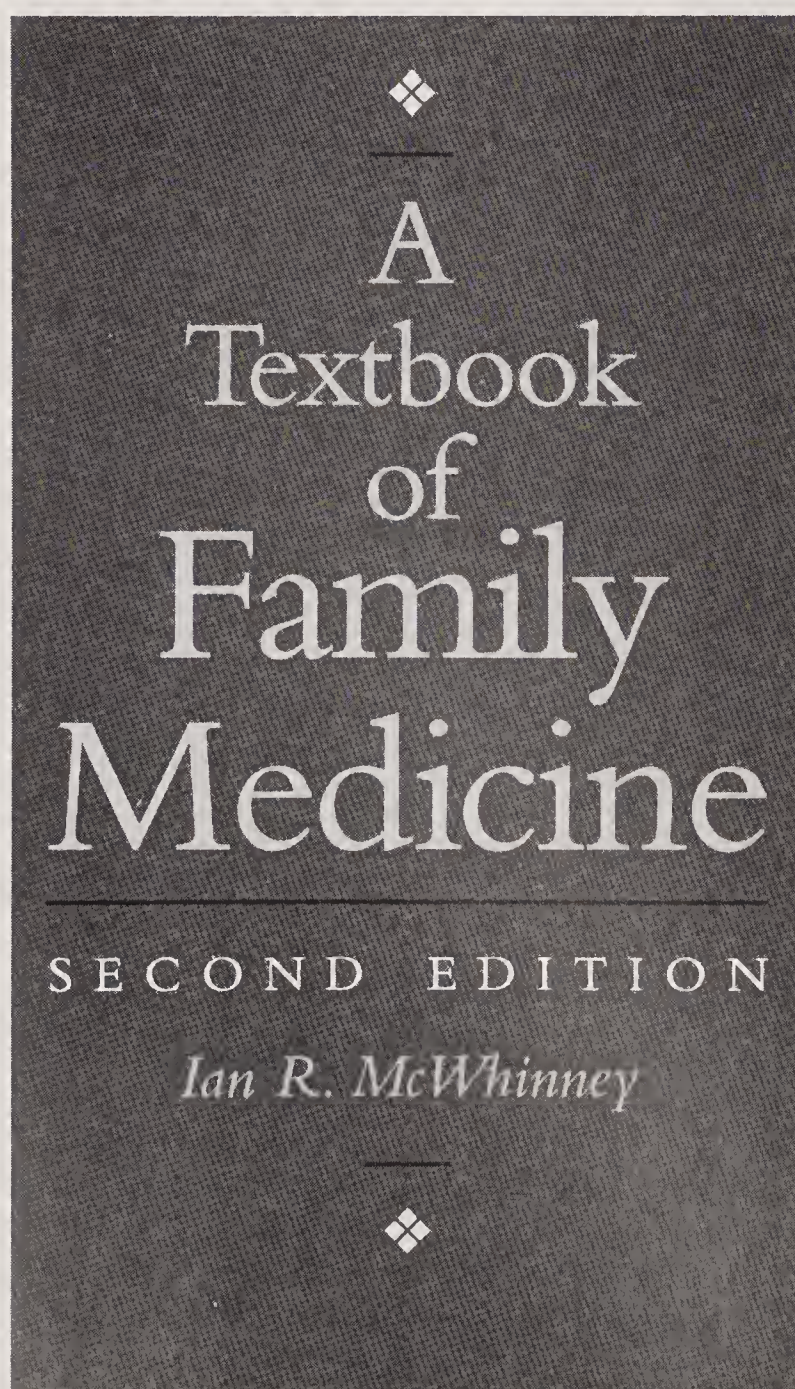
This advertisement was taken from the University of Toronto Medical Journal Archives.
UTMJ Vol. 20, p211, 1943.

A Textbook of Family Medicine, Second Edition

Reviewed By Stella Yiu, (OT1)

Written by: Ian R. McWhinney
Oxford University Press, 1997
Pages 448.

Overall Rating:	Good to Excellent
Strengths:	Comprehensive, practical information
Weaknesses:	At times, too much attention to detail on less important issues
Audience:	Family practitioners and students specializing in family medicine



In the preface of *A Textbook of Family Medicine*, McWhinney acknowledges that, in principle, family physicians should be available for any type of problem. There is thus no disease, however rare, that may not be encountered in family practice. One can therefore imagine the sheer volume of related material and will be impressed and amazed at how this book encompasses such information both concisely and appropriately.

The initial discussion of sociology and the history of medicine is not very interesting. At times, it is burdened with detailed statistics and principles. I imagine such information is helpful to students intending to specialize and those already working in family medicine, but it is not immediately relevant to a first year student.

Other than this somewhat disappointing start, I find "Doctor-Patient Communication" to be highly relevant and practical. McWhinney gives abundant examples in relation to interviewing, listening, empathy, difficult relationships, reassurance, and breaking bad news. Such discussion serves as a solid introduction to medical students and as continuous education for practitioners. The material is updated and backed by extensive research. The author includes patient-centered clinical method, diagnostic and problem-solving processes, with learning methods which are easy to understand and seem both efficient and effective. He also eloquently demonstrates the concept of "family" in family medicine. Whether it be family life cycle, high-risk signals in mothers, divorce, bereavement, or poverty, these issues are all discussed in appropriate length with solid references and great insight.

McWhinney devotes a large chapter to the preventive procedures for specific conditions. These conditions range from abdominal aortic aneurysms and cystic fibrosis, to par-

enting problems and ventricular septal defects. Even with the obvious difficulty in including every condition, this section gives concise, preventive measures for many diverse diseases. Such organized information alone makes this book a good immediate resource for family practitioners.

Part II deals with common clinical problems, including acute sore throat, headache, fatigue, hypertension, and diabetes. The discussion includes extensive but clear strategy for management, diagnosis and assessment, and other related clinical problems. Once again, the details are well referenced and concise. I only wish more common symptoms were being analyzed and dissected in such clear manner.

The third part discusses the daily practice of family medicine. With the current health care system in great flux and

the focus shifting more towards community and home care, this section seems highly appropriate. McWhinney discusses home visits, how to assess home care patients, and the new technology available. He also refers us to the changing roles of the members of the multidisciplinary health care teams, namely nurses, occupational therapists, social workers, clinical psychologists, behavioural therapists, dietitians, and pharmacists, and emphasizes the "team" concept. Also, family practitioners are made aware of the many different community resources, so they can then refer to such routes if they are deemed suitable.

Thus, I strongly recommend this book since it not only serves to provide a solid background for students in family medicine, but it is a valuable and up-to-date reference for family practitioners.

In Erratum

The *UTMJ* wishes to correct an error made in an article published in Volume 75, Number 3.

Correct authorship for
"Diagnostic Radiology: Functional Imaging," is:
Robert Yu, BSc. and Masanori Ichise, MD.

The *Journal* apologizes for any inconvenience this may have caused the authors.

INSTRUCTIONS TO AUTHORS 1997-1998

The University of Toronto Medical Journal (*UTMJ*), an official journal of the University of Toronto Faculty of Medicine, is devoted to the publication of significant, original studies and review articles in all areas of basic, clinical, translational and epidemiological medical research, as well as medical education, medical ethics, medical jurisprudence, and the history of medicine.

Procedure for Submission

Contributions should be addressed to: The Editors, *UTMJ*, Medical Sciences Building, Room 2141, 1 King's College Circle, University of Toronto, Toronto, Ontario, M5S 1A8, Canada; Phone: (416) 946-3047. The paper should be submitted by an author, preferably the principal author, who should indicate in a covering letter:

1. that the paper is being submitted for consideration for publication in *UTMJ*;
2. the exact address to which all related correspondence should be sent and the telephone and FAX numbers at which the author can be reached;
3. that neither the submitted manuscript nor any similar paper, other than an abstract of preliminary communication, has been or will be submitted to, or published, in any other primary scientific journal;
4. that all of the authors are aware of, and agree to, the content of the manuscript and that authorization has been given to use any information conveyed by either personal communication or release of unpublished experimental data;
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Journal article

1. Reinders FX, Chalin C, and Meier HMR. (1993). Alzheimer's disease: Understanding the patient and caregiver. *UTMJ*. 70(20): 16-20.

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2. Norris KE, Norris F, and Brunfeldt K. (1980). Nucleic Acids Synthesis: Applications to Molecular Biology and Genetic Engineering. Koster H (ed). IRL Press: London, pp. 233-241.

Books, theses, or comparable publications

3. Pressaco J and Yu H. (1996). Pharmacological Treatment of Diseases. Urban Angel Medical Books Inc: Toronto.

Tables

Tables should be on a separate page with a short title, and be numbered and referred to in the text. Column headings and descriptive matter in table should be brief. Vertical rules should not be used.

Illustrations

Each figure should be designed to fit into an area of either one or two columns of text. Photographs and illustrations must be in black and white and of good quality. The figures, including halftones and photographs, are to be numbered consecutively in Arabic numerals, and each one must be referred to in the text as Figure 1, etc. On the manuscript indicate with an arrow in the margin the most appropriate position for the figure. Figure legends should be on a separate, numbered page and titles for figure legends should be in the form of a concluding statement. Define all symbols and abbreviations used in the figure.

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Both non-proprietary (generic) and trade names should be provided for all drugs mentioned.

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University of Toronto Medical Journal
FOUNDED IN 1923 VOLUME 75, No. 1 DECEMBER 1997

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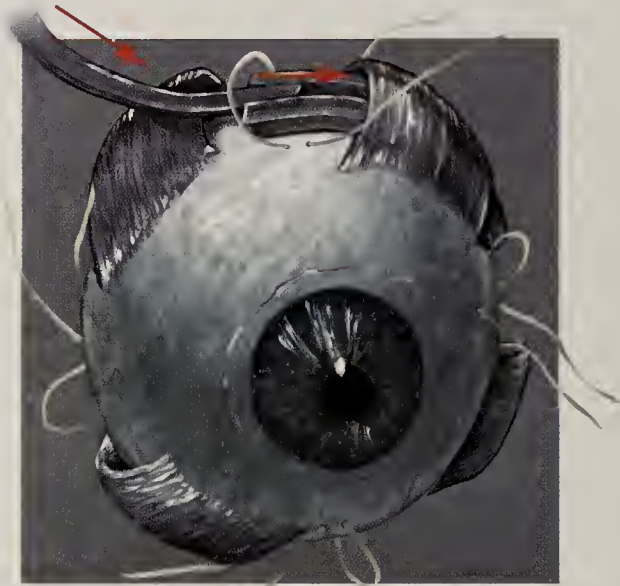
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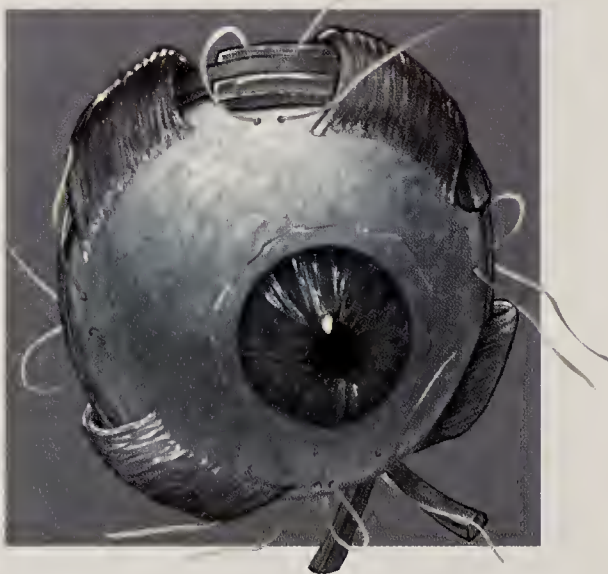
Retinal Implant Surgery



1



2



3



4

1. Implant inserts under muscle
2. Encircling band inserts through implant
3. Encircling band surrounds eyeball
4. Implant and encircling band sutured to eyeball